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An Address.[1]

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MAY I say how much I appreciate the honour I have received in being elected as the President of the Section of Orthopædic Surgery at this meeting of the Australasian Medical Congress—an honour conferred upon me, I take it, not because I am a practising orthopædic surgeon, but because I am one of the links in the chain whereby orthopædic surgery has come into being in Australia.

The two outstanding pioneers in orthopædic surgery in this country have been Sir Charles Clubbe, of Sydney, and W. Kent Hughes, of Melbourne.

The former, connected with the Children's Hospital in Sydney, was the first there to bring into operation the principles of orthopædic surgery in the rectification of deformity, especially that of club-foot, and of tuberculous bones and joints; and the latter did the same in Melbourne at the Children's Hospital, and in "Walsham's Surgery", which was the textbook for students of surgery in my generation, his was the hand that wrote the section on orthopædic surgery.

In those days, and up to the time of the Great War, the term "orthopædic surgery" was confined to that form of work which the term orthopædic more properly describes, namely, the task of making the child grow up straight.

Up to that period it was in Great Britain and Australia the work of the surgeon at children's

[1] The President's address, delivered before the Section of Orthopædic Surgery at the fifth session of the Australasian Medical Congress (British Medical Association), August, 1937.

hospitals, and they were the only surgeons with the knowledge of, and imbued with, the principles that would prevent deformity arising either from disease or after accident, and able to remedy it once it had been established.

These surgeons at the children's hospitals then carried out their work quite efficiently, and still, in most children's hospitals, continue to do so as part of their routine work, of which, in fact, it occupies nearly 50%.

In the United States of America and on the Continent the scope had been enlarged, and there were positions at the large hospitals for men who were orthopædic surgeons only, and adult work was included in its scope. But it was not until the Great War of 1914-1918, owing to the enormous number of wounded who needed treatment by orthopædic principles and methods, that this class of surgery jumped into existence as a surgical specialty in Great Britain and Australia. Before then there had been a few free lances in Great Britain, but they were not generally recognized by the profession as a whole. Notably amongst these were H. O. Thomas, of Liverpool, and his successor and nephew, Robert Jones, and also surgeons attending the National Orthopædic Hospital in London—Little, Tubby and others. In the early part of the century, however, Robert Jones had attained a world-wide reputation, and his clinic at Liverpool was a Mecca for all those from overseas interested in orthopædic surgery. Yet his existence was unrecognized in the great metropolis, and his rôle as a prophet was still unforeseen in his own country. It needed the catastrophe of the Great War to draw attention to his work and to the need of orthopædic principles in the treatment of the wounded; and we can all, those who knew him then and those who have known him since, appreciate what he did and what his methods did for the crippled soldier.

In the Great War the need for orthopædic measures in the treatment of the after-effects of gun-shot wounds especially was great, and an investigation made in Sydney showed that 80% of the returned wounded needed specialized orthopædic treatment for the deformities and disabilities that had arisen, many of which might have been averted had these principles been set in operation during the more acute stages. In Great Britain the need was recognized comparatively early, and Robert Jones was called upon to organize the orthopædic work there. How well he carried this out, there is no need to tell. It was not, however, until July, 1918, in spite of repeated appeals, that any effort was made in this country to organize similar work.

However, the impetus given at that time and the recognition of the need for employing those principles on which orthopædic surgery is based, have caused a flow—one might even say a flood—of orthopædic surgeons both in Great Britain and Australia, the installation of special orthopædic departments in large hospitals, the teaching hospitals in particular, and the recognition of orthopædic surgery as a distinct specialty, the scope of which is now enough and more than enough to occupy the attention of the surgeon to the exclusion of other types of surgery.

It might be asked at the moment whether the supply in this country or certain parts of it has not outstripped the demand, and whether the emoluments to be gathered under the present system justify the number of orthopædic surgeons. It might further be asked whether we are giving the best service to the public by having many departments at hospitals, both great and small, and by the holding of multiple posts by one man in several hospitals, or whether the work should be concentrated in one department of the teaching hospitals connected with the universities. In the former case we have small departments, scattered and tending to overlap with others, and in the latter concentrated service devoted to one thought alone. This, however, is a problem for the future.

The specialty of orthopædic surgery is an entrancing one, and, in spite of the number of orthopædic surgeons already existent, more and more are entering the field, and are travelling overseas to acquire the higher degree in that subject at Liverpool, and to enlarge their knowledge by attending clinics on the Continent and in the United States of America.

When orthopædic surgery became an entity in Great Britain, Sir Robert Jones had to define its scope, and it was seen to cover an enormous field; more has since then been brought within its ambit. A broad outlook must lead to the conclusion that orthopædic surgeons have taken such a large section of surgery that one person cannot be efficient in all portions of it. As our knowledge of medicine becomes greater and greater, and this rapid development can be noted even every month, so it becomes more and more impossible for one man to keep abreast of every phase that is still included in the scope of orthopædic surgery; it is altogether too much for the average brain to carry or, at least, to learn and execute satisfactorily.

The need for splitting up orthopædic surgery into subsections has become apparent. Whether the material available and the financial return for smaller specialties in such a small country as this are sufficient for such a splitting is arguable. The installation of such subsections at the larger teaching hospitals or at a central hospital would, however, undoubtedly be for the good of the people. Thus the question in a country like this of whether we should have many departments in many hospitals or a central orthopædic hospital in each State, is an important one.

But can we in any way forecast the future of the orthopædic surgeon?

Orthopædic surgery is now recognized as an entity, a specialty, and it is having the same tendency as all the others, of setting itself aside in its own special cell, and of divorcing itself in the main from the general wider interests of the profession. There is no question at all but that specialization has come because the need for it has

been shown to exist; and it is equally certain that the man who is a universal specialist, or who tries to do a bit of everything, gives less good service than the man who devotes all his time to acquiring knowledge of one of the smaller subjects in detail. However, on the other hand, there is the risk of the various specializing bodies getting into very narrow grooves of specialization, both by their training, and by shutting themselves up in a small cell apart from everybody else. The probabilities are, I take it, that some means will have to be devised which will overcome both of these difficulties.

In the days of the generation just gone by the method of training of the specialist was an ideal one. Most of those men had originally done some work in general practice, that work which gives the wide purview of after-results, but seldom seen in a hospital. They have then taken on general surgery, and, while undertaking that, have had their interests turned towards some special line of work, and later have given up their general surgery to become specialists in this branch. The present-day phase is for a young man to decide that he will become a specialist in one line or other; after a year or two years as a house surgeon he acquires a higher degree, usually on the other side of the world, and on his return acquires a post as a specialist surgeon in one of the greater or smaller hospitals, and it is only then that he learns the practical side of the work.

Now, this form of training has two drawbacks. First of all it is a form of training which narrows the man's outlook from the very beginning; he does not have access to that wider knowledge of general surgery or of general medicine that is so necessary for everybody, however he carries out his work in later life. Secondly, the present form is that the acquisition of a higher degree or some slight experience in seeing others at work elsewhere, valuable as it is, is considered sufficient. I think the time will soon come when, before a man can acquire a position in a public hospital as a practising specialist, he will have to show both some previous academic study, as shown by higher degree or diploma, and also a record of a considerable period of practical work under supervision

How this wider training can be given is quite another matter. There are two possibilities. The first is that all intending specialists in the sub-branches of surgery should come to the hospital, either as assistant surgeons or clinical assistants, and be taught their general surgery, that their leaning towards some specialty should be encouraged, and that they should have every opportunity given them at the same time of acquiring knowledge in that specialty by attending the surgeons who practise it. Thus when they come to seniority they may be able to discard the general side which has given them a wider training and finally take on the specialty altogether. In other words, anybody practising a surgical specialty should be a general surgeon and should pursue a hobby which is his specialty, until, in his later life, that hobby becomes his life's work. That is one way of doing it; whether it is practicable is questionable at present, and only time will show whether it is necessary. But the need of the general training is obvious in the case of orthopædic surgeons who are called upon to undertake the care of persons injured in industrial accidents.

The other method that might be adopted is the formation of teams and units that are going to take on a wide view of a certain branch of surgery. The various components of that unit should meet together from time to time to discuss the cases from all points of view. In that way those who are working in what must be confessed is at times a narrow specialty, would acquire the broad outlook which is so necessary if the patient's interests are to be served.

The scope of what is called orthopædic surgery is a very large one. Already there is a tendency for it to split up into sections, and if that is so, the same problem will arise as has already arisen in regard to the greater question of general and orthopædic surgery. A man will tend to practise orthopædic surgery as a whole, with a tendency towards one special line of it, that is, his hobby of the general part. And though he will learn and be trained as a general orthopædic surgeon, so, too, he will have to specialize in later years in one branch.

Three quite definite branches can already be visualized: the first, of children's orthopædic surgery; second, the surgery of accidents, whether they be of the industrial type or not; and already there is separating out itself another branch, that of fractures. Orthopædic surgery, as the name states, is intended to ensure by various means that the child grows up straight. First it was used to correct by surgical methods deformities that had arisen; but now it means a great deal more. In order to attain its ideal there must be taken into consideration, first, prophylactic measures that will cope with preventible deformity, so that children may be brought to healthy adult years; and the subject is so intermingled with the science of pædiatrics that it should be not divorced from the care of children. I think, therefore, that orthopædic surgery should be directed from a children's hospital, which is the only place where such work can be done on a large scale. These various aims can be combined only in what is termed a team or unit, in one big department that can control all these interests, both prophylactic and curative, that are so closely intermingled.

Everything in industry has become mechanized, and the average human brain has not yet learned to think quickly enough to enable men and women to keep pace with modern machinery; motor car accidents and accidents due to industrial processes are a common occurrence. We thus have emergency surgery, much of it giving rise to orthopædic problems; but one can see also that many of the subjects of these accidents need the control of the general surgeon. As I said before, it is necessary, particularly in this type of accident, that the orthopædic surgeon should have had some training in general surgery if he is going to cope with the injury, and

not have to call in different specialists to do a job on every part of the body that may have been injured in the accident.

Then, again, most accidents have associated legal complications. Industrial accidents are under the *Workers' Compensations Acts* of the different States, and, again, civil litigation arises from other causes, particularly motor car accidents. In these cases a more specialized training is really needed for the surgeon who goes into court to give evidence. The evidence given in court by orthopædic surgeons differs in no whit from that of other medical men on other subjects, but we must confess that it renders us the butt of legal practitioners on account of contradictory statements any two of us make under oath. Moreover, surgeons render themselves open to the charge that they give evidence for the side that subpœnas them and pays their fees. This is a subject that we, as a profession, might well think worthy of consideration, to see if some remedy cannot be instituted, though after all it is but human nature to be partisan, though we, of all people, should in such cases be judicial. There should be some system of training in the proper giving of evidence.

The question that must arise in these industrial accidents is whether we are doing enough merely as orthopædic surgeons attached to a hospital if we do the repair work of this injury, or whether our work should not be enlarged into a unit of much greater scope.

As I have said, at a children's hospital the unit should be concerned with child metabolism, child growth, and the making of a healthy man, of which orthopædic surgery forms but a part. So, too, in all industrial accidents, should there not be a unit with a comprehensive point of view, in which the orthopædic surgeon will play his part? In fact, I think the orthopædic surgeon should be the governor of the unit, one who is concerned not only with the period of hospitalization, but with after-care in the physiotherapy department. Finally, some department should have care of the rehabilitation of the injured person, and help him to return to civil life, capable of working for a living, even though it may not be the same type of work as he was able to carry out formerly.

As regards fractures, we already find in Great Britain, as the result of the report of fractures by the British Medical Association, that special fracture clinics are being installed in greater numbers in larger hospitals. To anyone who has given thought to the subject, the need of these clinics is outstanding. It was proved by the inquiry held by the British Medical Association that the amount of permanent morbidity resulting from present methods of treating fractures is a reflection on us, a medical body. One need only refer to Böhler's fracture clinic in Vienna to see what can be done. The need for such a unit is clear and easily seen, but it must be a specialized unit. Not only must the medical head devote all his time to the particular work, but his colleagues and assistants also must be trained and employed for years; in the present system house surgeons stay for a few months, and most of the nurses are doing their course of training, uncertificated and constantly changing. The sisters and nurses should be permanent and fully trained in the use of splints, and all with their work well defined and known. This cooperation and specialization in work should go right through the unit, should include the X ray department, and, not least, the work of the operating theatre. It is a special department and needs to be staffed by a body of specialists, from below upwards, if the best service to the public is to be given.

Of course, it is not always in our power to say how the complete team must be constituted. Under existing conditions in our large general hospitals we have allowed (perhaps the reasons may be unavoidable) the nursing side to become mainly a training school, and the proportion of trained nurses to those in training is quite inadequate. We know there are many reasons why this has perhaps been forced on hospitals; but at the same time, if we wish to run a unit efficiently, we should lay it down that it cannot be done without a large percentage of trained nurses on the staff of the unit, that they should remain there for some long period, that everyone in the unit should be completely trained so that they are all working in close relationship, and that as far as possible the members of the unit should be reserved for the work of that unit, and should not be used for any other purpose in the hospital. This is an ideal system, certainly, but if we took a more forcible stand there is no reason why we should not be able to attain it. The system of the constant changing of nurses in the course of training and of doctors in the similar state, does not give efficiency to a unit. Though it is necessary to have the trainees of both kinds going through and learning in their turn each part of the work in the specialized departments in the hospital, still the responsibility of the case should not be in any way thrust upon them. They are students just passing through, and the responsibility and the real work must rest in the hands of fully certificated and fully trained nurses and of doctors who are not constantly changing.

As far as rehabilitation is concerned, whether by physiotherapeutic measures alone or by properly graded methods of reeducation, we have, in our conception of the work of an orthopædic surgeon, bitten off rather more than we can chew, taking up too much general work and not specializing enough in one direction.

These are but the ideas of an individual as to the future trend and scope of our work, and they will, perhaps, be put into operation to a greater or less extent as times goes on. In what way changes will come no one can determine; but one thing is plain—under our present honorary system it is impossible for a man to find time to control such an orthopædic unit as it should be controlled and at the same time earn a living. Does a nationalized service offer anything better?

SUBSTANCES CONTROLLING THE GROWTH OF IMPLANTED TUMOURS.

By WARNFORD MOPPETT, M.D.,
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PREVIOUS papers[1] [2] [3] have described a series of experiments in which mice bearing implanted tumours have been subjected to experimental therapy consisting of irradiation in association with other forms of treatment. Attempts were made to secure a favourable modification of the stroma reaction by means of a preliminary injection of tuberculin or preliminary heating of the tumour region with a diathermy current.[1] Attention was then given to the action of metabolic inhibitors, potassium cyanide or sodium iodo-acetate being injected before irradiation.[2] The above methods of preliminary treatment appear to increase the effect of X ray treatment but not to any very great extent. Six other substances, including a photo-sensitizer, hypericin, were tried; but no effect was observed except in the case of thyroxin.[3] The effect of the latter was found to be independent of X ray treatment, and one object of the present work was to investigate this action. Gilroy[4] has described favourable effects following the administration of thyroxin to tumour-bearing animals; she ascribed this result to the removal by excess catabolism of the amino-acids needed for building new tumour cells. Thyroxin is considered to have at least two varieties of action: the acceleration of metabolism (which may be obtained also by such substances as dinitrophenol), and the acceleration of amphibian metamorphosis, which may be obtained by a variety of iodine-protein compounds.[5]

The literature was also searched with a view to an investigation of some other endocrine product being made. The profound influence of the endocrine glands on normal growth suggests the possibility of a controlling action on neoplastic growth, but many experimental findings are indefinite, or even contradictory. Sannié and Alphandéry[6] give an excellent summary of the position, and they see little indication of any immediate practical value in the treatment of tumours by endocrine products. There appears to be some agreement, however, that the secretions of the reproductive organs have some influence on tumour growth. Gonadectomy,[7] if performed sufficiently early, reduces the incidence of mammary cancer in those strains of mice which normally have a high incidence of such tumours as the result of selective breeding. In such strains the administration of œstrin raises the incidence of breast cancer in females, and occasionally produces breast cancer in males.[7] There is some evidence that removal of the gonads, especially the testes, diminishes the growth of implanted tumours, whilst the administration of testicular extracts may stimulate their growth.[6] Clinically, the hyperactivity associated with pregnancy often has an accelerating effect, for example, on breast tumours, but this may be secondary to increased blood supply. On the other hand, it has been observed by Gilroy[4] and confirmed here that pregnancy in mice with implanted tumours exercises a retarding influence, possibly through embryonic absorption of food products. The activity of the gonad and other reproductive organs is controlled to a large extent by the pituitary, which should exert an indirect influence on tumour growth through such channels, whilst the presence of a growth hormone in the anterior pituitary raises the possibility of a more direct action on tumour cell growth. Ball, Samuels and Simpson[8] appear to have obtained clear evidence that removal of the hypophysis retards tumour growth in rats. Bischoff, Maxwell and Ullmann[9] consider that tumour growth is accelerated by administration of a crude extract of the anterior pituitary, whilst irradiation of the skull retards tumour growth presumably by deactivation of the pituitary. Tumours appear to absorb the hormones of the gonad-pituitary series, since their growth checks the œstrous cycle in mice. This is apparently not due to mere wasting, since hormone administration restores the cycle.[10] Engel states that the growth hormone of the anterior pituitary stimulates tumour growth; but there is some doubt as to whether the other hormones of the pituitary, particularly the gonadotropic hormone of the anterior pituitary, act in the same manner or as antagonists to tumour growth.[11] Engel's view is that the stimulating property of the growth hormone is diminished by gonadotropic bodies from urine, but not affected by pituitary gonadotropic bodies.

In conjunction with the further investigation of thyroxin already mentioned, it was decided to test the effect of administration of a simple alkali extract of the anterior pituitary to tumour-bearing mice. This extract contains both growth and gonadotropic hormones among others,[12] but it is considered to be more powerful and constant in action than purified extracts, one of which was tried later.

Extraction of Pituitary Hormones.

The method of extraction described by Evans, Meyer and Simpson[13] was followed. Frozen ox pituitary glands were supplied by the abattoirs and 143 grammes of tissue were obtained when the anterior lobes were dissected out. The material, kept near freezing point, was minced in a small tissue mincer and added to 530 cubic centimetres of cold distilled water, the mixture being stirred for three-quarters of an hour. A further 215 cubic centimetres of distilled water were then added, followed by 200 cubic centimetres of 0·2 normal barium hydroxide solution, and the mixture was allowed to stand overnight in the ice chest. It was then centrifuged four times, after which 0·2 normal sulphuric acid was added to bring the pH to 8, phenol red being used as an indicator. The mixture was again centrifuged, 5·3 cubic centimetres of cold, saturated sodium sulphate solution were added to remove any barium not already precipitated, and the whole was centrifuged once more. A clear red solution is described by Evans, Meyer and Simpson,[13] but this product was a cloudy red liquid. It was stored frozen in shallow trays.

Test of Activity of Extract.

The activity of the pituitary extract was tested according to the method of Evans, Meyer and Simpson[13] by observing the increase in weight following its injection into a series of adolescent mice. The test was actually carried out after most of the work with tumours, in order to be sure that the activity was retained throughout such work. Two groups of ten mice were selected, and each mouse was weighed twice a week until the average weights became constant with the cessation of normal growth (Figure I). Then in one series the pituitary extract was given intraperitoneally in daily doses of 0·3 cubic centimetre for three weeks (Saturday and Sunday excepted), and the bi-weekly increase in the average weight is well shown by the continuous curve in the figure. The break in the

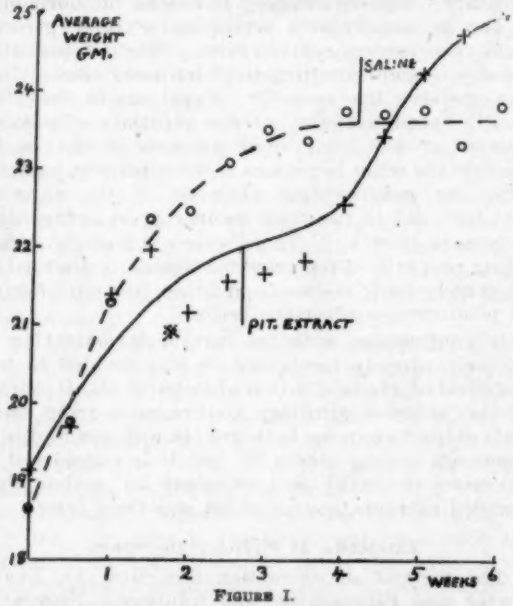

FIGURE I.

Growth curves with pituitary extract, continuous line; controls, broken line.

curve marked * was probably due to lack of food or water over a week-end. The control series of ten (reduced to nine by a death) were given a similar daily injection of saline solution after cessation of normal growth, and as shown by the dotted line in the figure, there was no further increase in weight. It will be seen from the figure, which is the result of 254 weighings, that the pituitary extract caused about 10% increase in the average weight. Evans, Meyer and Simpson describe a similar result when rats are injected with one cubic centimetre of their extract. From the rat/mouse weight ratio, the present preparation had lost about 50% of its activity; the cloudiness already mentioned and the lack of facility for cooling in the centrifuge would be in accord with such a loss.

Experiments with Tumours.

The mouse tumour S37 was implanted into a series of white mice, and about a week later the size of each growth was estimated by palpation. In the first series of experiments (Table I) fifteen mice were sorted out into three groups, "control", "thyroxin" and "pituitary", so that the average initial size should be the same for each group. Pituitary extract was given daily (Saturday and Sunday excepted) in doses of 0·3 cubic centimetre intraperitoneally until ten days after the first measurement, when all tumours were dissected out and weighed. The last three columns in Table I give these weights, whilst the fourth, fifth and sixth columns give the ratio of the final to the initial diameter, as previously described.[1] Unfortunately, as shown by the gaps in the table, there was a number of deaths, and two further groups of experiments were carried out before an average was calculated. It will be seen that the pituitary extract appears to stimulate tumour growth, the average weight being 2·44 grammes as against 1·66 grammes for the controls. These results are summarized in Table II, A, in which the increased average weight of the treated tumours is expressed as a difference, + 0·78 gramme, whilst an attempt is made to indicate the reliability by applying standard statistical formulæ for a difference of the two arithmetic means. Such a formula takes no account of the improvement in reliability which must result when the early tumours are sorted into pairs to give an equal average "initial size" for experiments and controls (Table I). This is obvious, if one takes an extreme case in which the vertical columns vary greatly and the horizontal differences are very consistent. However, when the "initial sizes" in a vertical direction do not vary greatly and it is justifiable to employ an arithmetic mean, it is reasonable also to employ the formula. The results are really a little better than they appear, but it is impossible to say how much better without knowing exactly how the performance of the inoculum in the first five or six days is related to the growth in the following ten days. Hence, in this work a result is considered to be significant if the magnitude is three times the error as above.

To facilitate presentation, the thyroxin results will be described later, and the next results with pituitary extract are summarized in Table II, C. Here the pituitary extract was given as before, except that administration commenced on the day the tumour was implanted. For the first four to five days the tumour cannot be palpated, but the original inoculum is being vascularized by the parent tissues.

Initially there were ten controls and ten injected animals, but deaths (and the omission of a control which failed to "take") reduced the numbers to seven and five respectively. In this type of experiment it is not possible to select groups of even growth rate by making an initial measurement, and the error is increased. The apparent stimulation, 0·26 ± 0·12 gramme, adds weight to the previous result although it is scarcely significant by itself.

The results confirm the findings of Bischoff and others,[9] but the effect may be due either to the gonadotropic hormone or to the growth hormone, or to both. Accordingly, an attempt was made to

purify the extract and to isolate the growth hormone by a method of Evans, Meyer and Simpson.[13] The dissolved matter was first precipitated as greyish white powder by means of acetone. This powder is stated to be stable at room temperature while it is dry. The growth hormone was isolated by treatment with glacial acetic acid, which gave a brown powder. Unfortunately this product proved very insoluble, and there was no opportunity to carry out a growth test. Some experiments with tumours (administration of the powder daily in 1% sodium bicarbonate solution) are summarized in Table II, D. The error is too large to allow the result to be significant.

TABLE I.

Comparison of Thyroxin and Pituitrin with Controls.

	Initial Size. (Millimetres.)			Ratio of Final to Initial Diameter.			Final Weight. (Grammes.)		
	Control.	Thyroxin.	Pituitary.	Control.	Thyroxin.	Pituitary.	Control.	Thyroxin.	Pituitary.
A		4	4		4	5		0·96	2·63
		2	1	Unreliable				1·72	1·70
	4		4	2·5		6	0·46		2·81
	3	3	3	7	5	5	2·35	0·75	1·78
	2	3	2	9	5	11·5	1·51	1·21	2·68
B	3	3	3	4	7·5	7	0·33	1·82	1·59
	4		4	5·5		6	2·05		3·32
	2	2·5		9	10		1·82	2·50	
	3	3	3	8	7	7	2·21	1·47	2·09
C	3	3	3	7	5	9	2·05	1·49	4·94
	8	10	10	2·5	2	2	2·43	3·33	2·41
	2·5	2	2	8	9	9	1·70	1·46	1·97
	3	2	2	6	8	7	1·33	1·16	1·31
Average	3·41	3·41	3·42	6·23	6·25	6·77	1·66	1·62	2·44

Blank spaces indicate death of animals.

TABLE II.

	Treatment.	Number Surviving.	Average Initial Diameter. (Millimetres.)	Average Ratio Final to Initial Diameter.	Average Final Weight. (Grammes.)	Difference of Averages (Means). (Gramme.)	Probable Error of Difference of Means.
A	Crude pituitary extract	12	3·42	6·77	2·44	+0·78	±0·25
	Control	11	3·41	6·23	1·66	Nil	±0·22
	Thyroxin, 3 doses	11	3·41	6·25	1·62		
B	Thyroxin, single	5	2	6·75	1·09	−0·59	±0·36
	Control	5	2	7·50	1·68		
C	Crude pituitary extract	5	Treatment		0·57	+0·26	±0·12
	Control	7	from time		0·31	Nil	±0·04
	Thyroxin, 3 doses	6	of implant.		0·34		
D	Treated pituitary extract	9	3	4·13	0·86	+0·19	±0·21
	Control	9	3	3·06	0·67		
E	Thyroxin, single, tail	4	3	5·6	0·87[2]		Error large.
	Thyroxin, single, dorsal	4	3	5·9	1·31		
	Thyroxin, 3 doses, dorsal	4	3	5·1	0·97		
	Thyroxin, daily, dorsal	2	3	7·0	1·85		
F	Thyroxin, single, at implant	4	7[1]	3·5[3]	2·54		Error large.
	Thyroxin, implant + 6th day	4	5·25[1]	4·5[3]	1·46		
	Thyroxin, single, at 6th day	4	6[1]	3[3]	1·10[3]		
	Control	4	7·25[1]	4·1[3]	2·48		
G	Dinitrophenol, 3 doses	6	1·7	5·3	1·73	−0·44	±0·26
	Control	9	1·8	7·4	2·17	−0·51	±0·30
	Thyroxamine, 3 doses	10	1·7	5·7	1·66		

[1] 6 day size. [2] Ratio $\frac{16}{6}$ day size. [3] Lowest value.

Experiments with Thyroxin.

Turning to Table I it will be seen that experiments were carried out with thyroxin in conjunction with the work already described. The tumour-bearing animals received 0·1 cubic centimetre of 0·1% thyroxin in saline solution subcutaneously in the dorsal region. This dose was repeated three, and again six, days later. Table II, A, which gives the results, shows that the injection had no effect when comparison is made with the controls. This was unexpected after the retarding effect recorded previously.[3] On the former occasion a single injection of 0·05 cubic centimetre was given subcutaneously in the tissues of the tail. The thyroxin is absorbed slowly from such a site, whilst its action is prolonged over several days, though gradually diminishing. In the present case the treatment was much more intensive, and the average initial size of the tumour was larger—3·41 millimetres as against 3·1 millimetres. Gilroy[5] has noted that large tumours do not respond to thyroxin, and accordingly a check series of experiments was carried out by giving a single dose (0·1 cubic centimetre) of thyroxin solution subcutaneously in the tissues of the tail when the average tumour diameter was 2·0 millimetres. (See Table II, B.) This result shows a retardation of growth, but it is not significant, as the "error" is 3/5 of the effect. If, however, this result is taken with that of a previous paper,[3] a difference is found of 0·71 ± 0·28 gramme for thirteen experiments. This retardation, 33% of the control value, is just about significant.

There were obviously several variables to be investigated, and in the next experiment very intensive treatment was given, 0·15 cubic centimetre being injected subcutaneously in the dorsal region at three-day intervals, as in Table II, A. Now, however, the first injection was given with the implantation so as to include the organization and early growth of the tumour (see Table II, C). The results were negative, the average weights being practically the same and the error was only ±13% of the control value. It appeared as if the mode of administration determined the result.

Accordingly four groups of animals were selected, so that the average initial tumour size in each group was three millimetres (see Table II, E). One group received a single injection of 0·1 cubic centimetre subcutaneously in the tissues of the tail, another group received a similar injection in the dorsal region, a third group received similar doses in the dorsal region at three-day intervals, and the last group received daily treatment. The error here is very large, but it will be noted that the single injection in the tail tissues gave the lowest result.

A further attempt to clear up the problem is recorded in Table II, F. Here there were four groups, a control group, a group receiving 0·1 cubic centimetre dorsally at the time of implantation only, another group receiving a dose at implantation and another six days later, and the fourth group receiving a single dose at the sixth day. The results show that a single injection at the sixth day is most effective. These results support previous findings, but the error is very large with such small numbers.

The probable meaning of the foregoing results is that there are an optimum tumour size, an optimum intensity of treatment and possibly an optimum rate of absorption, when the tumour-bearing animal is treated with thyroxin.

The Two Actions of Thyroxin.

Another aspect remains to be considered, the possible separation of the two actions of thyroxin; these are the stimulation of tissue metabolism and the "organizer" effect on tadpoles. Gaddum[14] confirms the results of Swingle, Helff and Zwemer that certain derivatives of thyroxin accelerate the metamorphosis of tadpoles, but he ascribes this action to the release of iodine. This is obviously not the action wanted, but in a later paper Gaddum[15] states positively that a derivative "thyroxamine" has no effect on oxygen consumption. Abderholden and Wertheimer[16] state that thyroxamine causes metamorphosis in axolotls. Accordingly, thyroxamine was obtained, with a view to testing a possible "organizer" action on tumour cells.

Thyroxamine proved to be very insoluble, but finally a suspension of 1 in 10,000 in saline solution was prepared. In order to give a dose comparable with that of thyroxin, one cubic centimetre was given to the tumour-bearing animals (see Table II, G). This large injection was given under the loose skin on the dorsal region, and it was repeated three, and again six, days later, because it was not known whether thyroxamine would have the prolonged action of thyroxin. The control animals in Table II, G received one cubic centimetre of saline solution after the above procedure. At the same time, a third series of tumour-bearing animals received dinitrophenol, which is a stimulant of tissue metabolism without any "organizer" action. In these experiments one is inclined to seek a clear-cut result by giving massive doses. Accordingly, 0·5 gramme of dinitrophenol *plus* 0·5 gramme of sodium bicarbonate was dissolved in 100 cubic centimetres of water, and the mice received 0·1 cubic centimetre of the solution dorsally. This would be proportionately about three times the maximum dose given to man, and it proved too toxic, since three animals promptly died. Further doses of half the above amounts were given at the third and sixth days.

Both substances appear to diminish tumour growth (see Table II, G), but the results have little significance owing to the large errors. There is an indication for further work, particularly with thyroxamine.

Discussion.

In confirmation of the conclusions of Bischoff and others,[9] it appears that crude extracts of the anterior pituitary, containing both gonadotropic and growth hormones, stimulate tumour growth. The finding with a purified growth hormone preparation was indefinite. It would be of great theoretical importance if the growth hormone was shown to influence tumours, since the tumour cell is in most ways free of those controlling influences which come either from adjacent tissues or distant endocrine

glands and determine the scope of normal tissue growth. Unfortunately, in the case of the growth hormone, and also in the case of œstrin and its related carcinogenic substances, the stimulating effect is the opposite to that required in cancer treatment. Thus there is little scope for practical application, except that in special circumstances irradiation of the pituitary or ovaries might hold a growth in check. There appears to be scope for a systematic study of the effect of endocrine administration, or graft, and also of deprivation by operation or by X rays in those strains of mice which have been bred to give a high incidence of spontaneous tumours.

Thyroxin is notable among endocrine products in retarding tumour growth. This effect is not very pronounced, nor have all results been consistent, but in certain circumstances Gilroy's findings have been confirmed. The problem of its action has not been solved, but the first question to consider is whether thyroxin retards tumour growth, because of its general stimulation of metabolism. Gilroy's hypothesis that available foods are removed by excess catabolism is not supported by her observation that large tumours do not react to thyroxin. It appears that mice are resistant to thyroxin, and previous tests[3] failed to reveal an appreciable loss of weight after its administration. Hence the general effect cannot be great, but it is difficult to prophesy what would be the effect on the tumour cells. They might become "thin" like a susceptible animal, or they might be stimulated to more rapid growth, and inconsistent results might be due to opposing influences. Since the tumour cells are mouse cells, they are probably resistant. Moreover, tumours are independent tissues, and Needham has drawn attention to the fact that isolated tissue slices are not affected by thyroxin.[17] The results obtained here with dinitrophenol (if valid) may be interpreted in various ways, possibly as a general toxic effect, possibly as a stimulation of metabolism. It would be of far greater importance to obtain a positive result with thyroxamine, provided that Gaddum's statement that no increase in oxygen consumption was obtained can be interpreted as evidence that thyroxamine does not stimulate metabolism after injection. Undoubtedly one can regard a tumour as in some respects a dedifferentiation. In the early embryo differentiation is believed to result, partly at any rate, from certain definite chemical molecules termed organizers. In certain amphibian embryos, a second neural canal can be brought about by certain ether soluble substances which are probably related to cholesterol and to the cancer producing molecules.[18] One would expect an organizer to retard tumour growth by causing differentiation of the tumour cells, and thyroxin may be considered in this class of substance in virtue of its action on amphibian metamorphosis. There is thus a prospect of controlling cancer growth by administration of organizers. One would not expect success in every case with a given substance, since organizer action depends on "competence" of a given tissue to respond. Nevertheless, if thyroxamine or a more potent derivative, or some of the cholesterol derivatives, would control any recognizable tumour, a new era in cancer treatment would be introduced.

Conclusions.

1. It has been found, in agreement with the conclusions of other workers, that extracts of the anterior pituitary containing both growth and gonadotropic hormones appear to stimulate the growth of an implanted tumour.

2. It has been found, in agreement with the conclusions of other workers, that thyroxin may in certain circumstances retard the growth of implanted tumours.

3. A suggestion is made for further work with thyroxin derivatives and other substances, which may have the properties of embryonic organizers.

Acknowledgements.

I wish to thank Professor H. Priestley for advice on the work and its presentation, Professor C. G. Lambie and Miss M. J. Spruson for help with the pituitary extract, Dr. F. Lions and Miss R. Harriden for help with the thyroxamine, and the Cancer Research Committee of the University of Sydney for assistance in carrying out this work.

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ACROCYANOSIS.

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INTRODUCTORY AND HISTORICAL.

ALTHOUGH acrocyanosis may be regarded as a trivial disorder of the peripheral circulation, devoid of serious consequences and causing little, if any, disability or discomfort to the patient, it is nevertheless of considerable clinical and physiological interest. Pathological anatomy and animal experimentation have so far thrown little light on the condition, and most of our knowledge regarding it has been obtained from clinical observation and experiment.

The two cardinal signs of the disorder—coldness and blueness of the extremities—are very commonly met with and may arise from a variety of causes, and it may be doubted whether it is justifiable to look upon acrocyanosis as a specific clinical entity. The term acrocyanosis was coined by Crocq[19][20] and was applied to a condition marked by permanent and painless cyanosis of the extremities, but with otherwise negative characteristics—absence of trophic changes, of contractures and of evidence of gross involvement of nerves. Previous to Crocq, Nothnagel[84] and Hoffmann[42] had each reported what may have been cases of acrocyanosis, but the first adequate description of the condition was given by Cassirer[12] in his monograph published in 1901. It was then differentiated from the disorder (or rather disorders) described by Raynaud[89] in 1862, and from erythromalalgia, which had been described by Weir Michell[82] as far back as 1872 and 1878. Later work has served to distinguish it from cyanosis associated with various forms of arteritis,[9] gross nerve lesions, respiratory and cardiac disease and abnormal conditions of the blood. A hypertrophic form of the disorder, characterized by thickening of the soft parts of the hands, was noted by Cassirer, and examples of this variety were subsequently reported by Kollaritz[56] and Kartje.[51] This form has to be distinguished from a certain condition, marked by cyanotic thickenings and occurring over the lower part of the legs, especially above the malleoli, or on the inner side of the knee and thigh or on the posterior aspect of the arm, which has been described under various captions, such as "strumous œdema",[1] "symmetrical asphyxial œdema",[99] "supramalleolar adipocyanosis",[27] or "erythrocyanosis".[88][98] Unlike acrocyanosis, erythrocyanosis does not involve the most distal parts of the extremities, nor are the cheeks, nose and ears affected.

With the exception of microscopic studies of the capillaries[4][5][31][38][39][83][87][110][111] very little was done to elucidate the mechanism of the vascular changes in acrocyanosis until the work of Lewis and Landis.[71] This work has been extended by Elliott, Evans and Stone,[29] while further contributions to capillary microscopy have been made by Kistiakowsky,[55] Kreindler and Elias,[58] Santori[92] and Flarer.[33] Physiological and clinical studies of acrocyanosis have also been published by Layani,[61][62] May and Layani,[78] Villaret, Justin-Besançon and Cachera,[107] and Villaret, Justin-Besançon, Cachera and Boucomont.[108]

As regards the essential cause of acrocyanosis opinion has varied. It was early claimed as an expression of glandular insufficiency. Thus Hertoghe[41] and Levi[64][65] regarded it as a manifestation of hypothyreoidism, Marañon[76] referred it to failure of the internal secretion of the gonads, while Hutinel[45] placed it among the pluriglandular dystrophies of adolescence. The view has been put forward that it is a disturbance of the nervous or neuro-endocrine control of the vessels.[73] Lewis and Landis,[71] on the other hand, consider that the fault is localized in the vessels themselves.

Acrocyanosis in its fully developed form is a sufficiently rare disease to warrant the recording of a single case. Its exact relationship with the milder and commoner forms of blueness and coldness of the extremities is uncertain, and therefore it is difficult to draw conclusions from such cases. It is therefore of importance to study the fully developed forms in their complete clinical context. The interest of the case here reported lies in the association of the typical and fully developed condition with disturbances of mental development, bodily growth and metabolism. The family history is also of interest.

CASE REPORT.

D.B., a single woman, aged twenty-one years, was admitted to the Royal Prince Alfred Hospital on October 3, 1936, complaining of coldness and blueness of the extremities and highly coloured cheeks, present since early childhood, of excessive thinness since childhood, and of the fact that the monthly periods had not appeared. According to the mother's statement, the patient's hands and feet had been cold and blue "since birth", while the complexion had always been florid, both in winter and in summer. The blueness of the extremities had been constant, but varied in intensity according to the temperature, being more marked in cold weather. It was not paroxysmal and the fingers never became blanched. The patient never experienced any pain, cramp, stiffness, numbness or other forms of paræsthesia. At the age of sixteen she first complained of chilblains, which she ascribed to being forced to use cold water in performing domestic duties. The chilblains on her fingers ulcerated; those on her toes did not. She was advised to wear woollen gloves and to use warm instead of cold water. Since doing so she has had no further trouble with chilblains.

She has been very thin since childhood and there has been some loss of weight during the past few years, although the exact amount is not known. Since 1931 she has experienced unwonted breathlessness and palpitation on walking fast up a hill or on running, and she has also had occasional attacks of giddiness; but an exercise tolerance test (bending down and touching the toes twenty times) yielded normal results. She has never complained of weakness or lassitude, nor has there been any swelling of the feet. She has never menstruated and she has no interest in the male sex. Apart from her present trouble she has never had any illness of any kind. There was no history of infectious diseases, cutaneous eruptions or rheumatic disease.

As regards the family history, one brother (aged fifteen), one sister (aged seventeen), her father (aged seventy)

ILLUSTRATIONS TO THE ARTICLE BY C. G. LAMBIE AND S. M. MORSON.

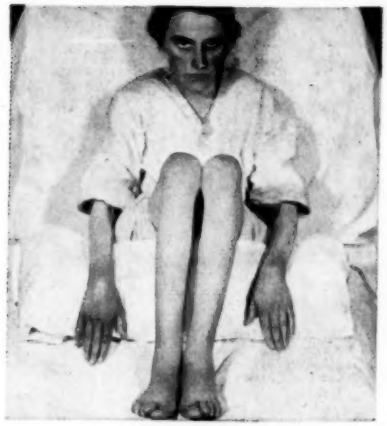

FIGURE III.
Patient D.B. immediately before injection of one cubic centimetre of pituitrin, showing distribution of cyanosis.

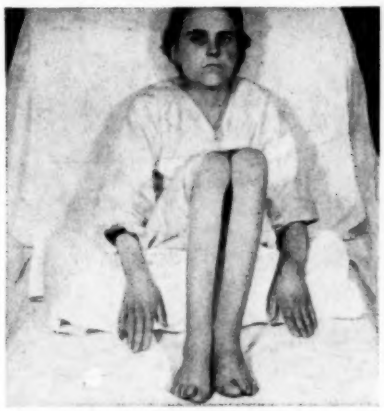

FIGURE IV.
Patient D.B. twenty minutes after injection of one cubic centimetre of pituitrin.

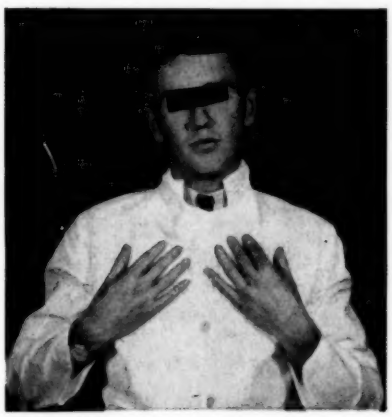

FIGURE V.
Control S.M. immediately before injection of one cubic centimetre of pituitrin.

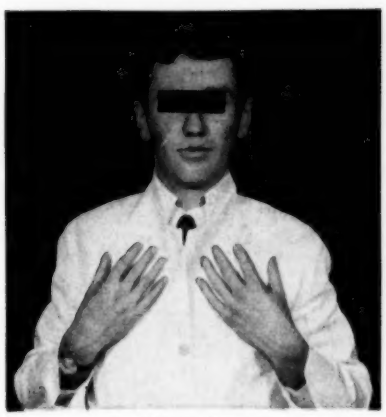

FIGURE VI.
Control S.M. twenty minutes after injection of one cubic centimetre of pituitrin.

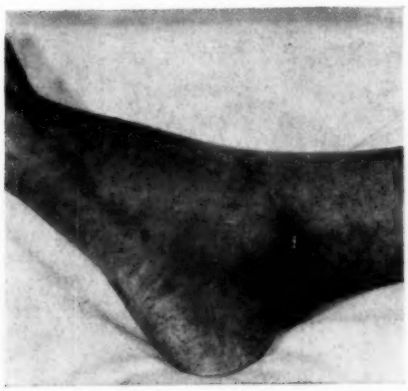

FIGURE VII.
Photograph of foot, showing cyanosis and mottling.

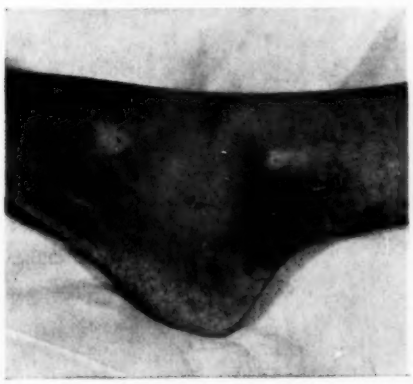

FIGURE VIII.
Photograph of foot twenty minutes after intradermal injections of pituitrin (above malleolus), histamine (over malleolus), adrenaline 1 in 5,000 (below malleolus).

ILLUSTRATIONS TO THE ARTICLE BY C. G. LAMBIE AND S. M. MORSON.

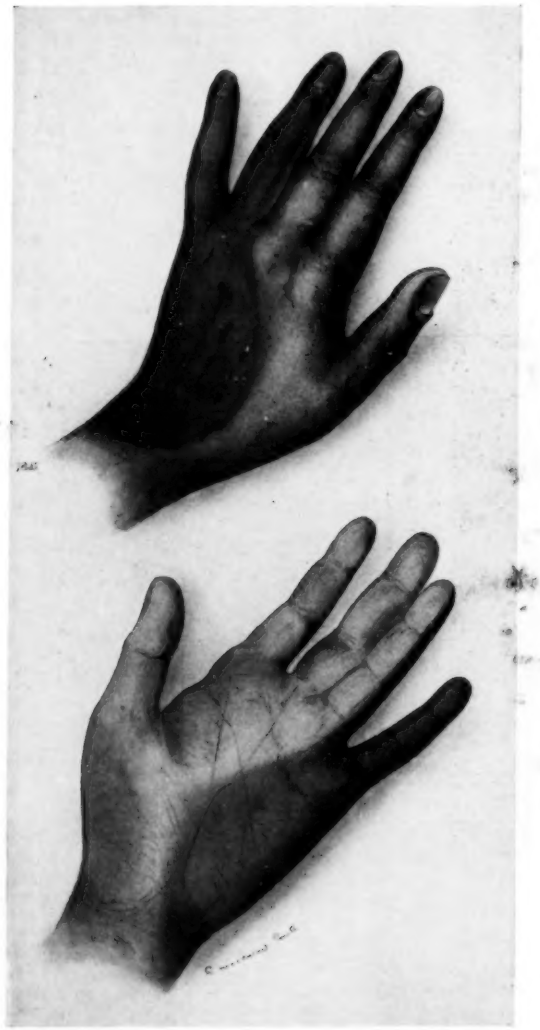

FIGURE XI.
Showing distribution of area of vaso-dilatation after ulnar nerve block.

and three uncles and one aunt on the father's side all complained of chilblains and of blueness of the extremities. Her mother had never had any miscarriages and there was nothing in the history to suggest syphilitic infection or birth injuries.

The patient lives a secluded and happy life at home in healthy surroundings. She has no men friends. Her chief amusement is going to the cinema.

Physical examination reveals a girl of puny physique and subnormal intelligence. Her face is thin and the trunk and limbs are emaciated. The cheeks (see Figure III) are of a deep violacious hue. The blueness extends onto the nose, but is not so marked here as on the cheeks. The ears and lips also exhibit slight cyanosis. The hands and forearm are of a dusky blue colour, darker in tint than the cheeks. The cyanosis is most intense at the tips of the fingers and gradually fades proximally. At

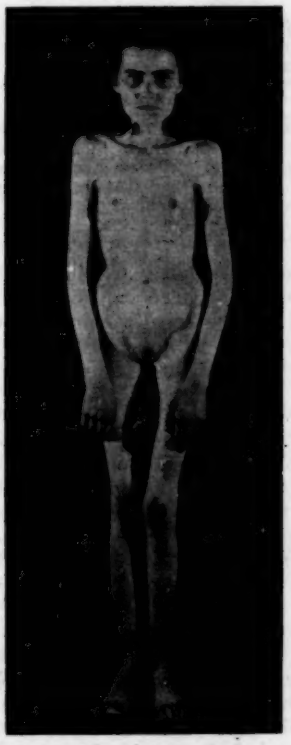

FIGURE I.

Ordinary photograph, showing distribution of cyanosis, emaciation, and lack of development, sexual and skeletal.

room temperatures of between 15° and 20° C. it extends almost up to the elbows, but at temperatures of between 20° and 25° C. it reaches only to about the middle third of the forearm. There is no sharp line of demarcation between the cyanosed and the normal skin, but after intermediate mottling the one merges insensibly into the other. At higher temperatures the blueness fades and the colour becomes paler and pinker. When the hands are dependent, the colour is much intensified and the veins swell. While the back of the hands, the dorsal aspect of the fingers and the palmar surface of the terminal and to some extent of the second phalanges exhibit marked cyanosis, the palm of the hand shows much less discoloration. At room temperatures of between 20° and 25° C. transient irregular patches of a red colour are occasionally seen upon a cyanotic background. The appearance of these patches cannot be related to emotional disturbance, but seem to be caused by transient pressure, such as contact with the bedclothes or other objects or by changes in the posture of the limbs. Apart from these transient flares the discoloration is almost homogeneous, with a faint suggestion of mottling, constant and symmetrical. The hands are cold to the touch, dry and scaly. There has never been any suggestion of hyperhidrosis. The fingers are gracile and do not exhibit any clubbing. The nails are well formed and there is no evidence of any trophic changes in the skin. Capillary pulsation is absent and the veins are not prominent.

The cyanosis of the feet and legs is somewhat less marked than that of the hands and forearms; otherwise it is of a similar colour and distribution. On cold days it extends almost up to the knees, while at moderate room temperatures it goes no further than one-third or half way up the leg. It shows a similar grading in intensity, increasing from the proximal to the distal portion of the limb. It is most marked at the tips of the toes and on the dorsal surface of the foot and great toe, while the sole of the foot is much less cyanosed. There is rather more mottling than in the upper extremities. This is well seen on the foot and leg. On the leg the cyanosis is most marked on the elevations round the hair follicles (see Figure III).

The feet are cold to the touch and, as in the upper extremity, there is a marked difference in temperature between the proximal and the distal portions of the limbs. The temperature gradients, as recorded by the thermocouple, may be seen from the following figures for skin temperatures at various points taken with a room temperature of 70° F.

Upper extremity—	
Tip of index finger	72° F.
Dorsum of hand	76° F.
Middle of anterior aspect of forearm	82° F.
Elbow	87° F.
Middle of anterior aspect of arm	90° F.
Lower extremity—	
Tip of great toe	70° F.
Dorsum of foot	72° F.
Middle of anterior aspect of leg	82° F.
Middle of anterior aspect of thigh	85° F.
Face	86° F.
Trunk (umbilicus)	92° F.

The skin of the feet and legs is dry and scaly, especially over the dorsum of the foot, where it is slightly chapped just below the ankle joint. The nails are thick and there is hyperkeratosis of the soles. The toes do not exhibit clubbing. There is no swelling or œdema of the ankles and there are no prominent veins or varices. Pulsation can be felt over the *dorsalis pedis* artery.

The wall of the radial artery is not palpable. The radial pulse rate is 72 per minute when the patient is in the recumbent posture; it is 78 per minute when she is standing. The rhythm is regular. The maximum blood pressure is 125 millimetres of mercury; the minimum blood pressure is 90 millimetres; the differential pressure is 35 millimetres of mercury.

The heart is not enlarged; the left border of deep cardiac dulness is encountered half an inch internal to the mid-clavicular line in the fifth interspace; the right border of deep cardiac dulness cannot be delimited by percussion. X ray examination shows that the shadow of the heart and great vessels is normal in shape and size. The heart sounds are clear and of normal intensity at each orifice and no murmurs are present. The electrocardiogram is normal.

No pulsations are visible in the neck and no prominent veins are seen in the limbs. As seen on the infra-red plate (see Figure II) the veins of the limbs and abdominal wall appear to be more distinct than usual, but this may have been due partly to the thinness of the skin and subcutaneous tissue. The venous pressure as determined by the direct method is normal, the fluid level in the burette being opposite the lower border of the *manubrium sterni*.

The oxygen capacity of the blood is 18·5 volumes *per centum*. The arterial blood contains 17·6 volumes of oxygen *per centum*, that is to say, it is 95% saturated. The venous blood taken without stasis from a vein at the elbow at room temperature 23° C. contains 6·0 volumes

of oxygen *per centum*, corresponding to an oxygen saturation of 32%. The arterio-venous oxygen difference in the upper limb is therefore 10·6 volumes *per centum*.

A blood count and hæmoglobin estimation yielded the following information:

Red cells, per cubic millimetre	4,180,000
Hæmoglobin, 13·6 grammes *per centum* = 94% of normal.	
Colour index	1·0
Reticulocytes	Less than 1%

The red cells show slight anisocytosis and polychromasia.

White cells, per cubic millimetre	5,200
Neutrophile cells	84%
Lymphocytes	10%
Monocytes	6%

The liver, spleen and lymphatic glands are not enlarged.

Examination of the nervous system shows that the patient's intelligence is subnormal, rendering her unfit for any occupation. Her memory is poor and she exhibits

FIGURE II.
Infra-red photograph, showing veins.

retarded cerebration. She spends most of her time reading, but she can remember nothing of what she reads. She is rather quiet and unemotional, but obstinate and stupid. Physical examination of the nervous system revealed no abnormality of sensation, of movement or of reflex activity.

Her height is four feet eleven and three-quarter inches; her weight is four stone seven and a half pounds. She is extremely emaciated. The ribs are prominent, the abdomen is scaphoid, the limbs are thin, and the bony prominences are much in evidence. The breasts are atrophied. The hair on the scalp and eyebrows is abundant, but the growth of hair in the axillary and pubic regions is very sparse (see Figure I). The distribution of the pubic hair is of the female type. There is an excessive growth of hair on the upper lip. The external genitalia are poorly developed. The patient refused to be examined *per rectum* or *per vaginam*. X ray examination shows that the pituitary fossa is small but apparently within the normal limits of size. There is no obvious thinning or other abnormality in the texture of the bones. The epiphyseal junctions are closed and the patient's bone age corresponds with the chronological age. The thyreoid gland is not distinctly palpable, but the rings of the trachea cannot be felt. The basal metabolic rate is −19%. The body temperature varies between 97° and 98·4° F., that is to say, it is slightly subnormal. The sugar tolerance is increased. The blood sugar curve after ingestion of 50 grammes of glucose is shown by the following data:

Blood sugar before glucose	88 mgm. %
Blood sugar half an hour after glucose	70 mgm. %
Blood sugar one hour after glucose	70 mgm. %
Blood sugar one and a half hours after glucose	97 mgm. %
Blood sugar two hours after glucose	79 mgm. %

The blood calcium is 8·0 milligrammes *per centum*, that is to say, slightly diminished. The urine contains no abnormal constituents. There are no abnormal signs referable to any of the other systems. X ray examination of the chest reveals no abnormality.

PATHOGENESIS OF ACROCYANOSIS.

Two distinct problems are involved concerning the pathogenesis of acrocyanosis. First, there is the question of the localization and character of the vascular changes, and secondly that of the underlying causes of these changes.

Localization of the Vascular Changes.

The fault might conceivably reside in any part of the peripheral vasculature—veins, subpapillary venous plexus, capillaries, arteries, arterioles, subpapillary arteriolar plexus or arterio-venous anastomoses—and it will be necessary to discuss the evidence bearing upon each of these situations.

Veins and Subpapillary Venous Plexuses.

Erben[81] and Parrisius[87] both attributed the condition to spasm of the veins. Erben considered that there was a "dissociation" between the tonus of the subcutaneous veins and that of the intracutaneous veins, the subcutaneous veins being poorly filled because of increased tone, and the intracutaneous veins overfilled owing to hypotonus. As Lewis and Landis[71] have shown, however, it is easy to demonstrate that the outflow of blood from the capillaries into the veins is not impeded. The hands are placed in a water bath at 30° C. for ten minutes, dried and placed together on a table at the level of the patient's heart, the subject being in the sitting posture. One hand is then elevated above the head and subsequently replaced beside its fellow after periods varying from two to sixty seconds. It is found that elevation for less than fifteen seconds causes distinct paling, while when the hand is lowered to the level of the heart several minutes (three or four) must pass before its colour becomes the same as that of the other hand. From this it may be inferred that the blood can freely leave the capillaries and subpapillary venous plexus, but can enter them but slowly.

While elevation of the limbs causes a prompt paling the limbs do not entirely lose their cyanotic colour.

Thus when the upper limbs of the patient herein reported were kept in the vertical position for ten minutes at room temperature (20° C.) increased mottling was observed, but the cyanosis was still marked at the end of this period. A similar change occurred in the lower limbs when they were placed at an angle of 45° to the horizontal for from ten to fifteen minutes.

Allowing the limbs to become dependent for long, as in standing or walking, had the opposite effect, namely, a deepening of the cyanosis, showing that the rise of pressure in the veins was freely transmitted to the subpapillary venous plexuses and the capillaries.

That the capillaries and subpapillary venous plexuses can fill readily from the veins and adjacent subpapillary plexuses, but not so readily from the deeper afferent vessels, is shown by the following test. With the patient in the recumbent posture pressure was applied with the point of the finger to the skin on the dorsum of the hand and foot. In each situation the colour returned to the area blanched by pressure within the normal period, namely, four to five seconds; but the colour was observed to return only from the periphery.

Lewis and Landis[71] have brought forward further evidence that there is no obstruction on the venous side by showing that if the capillary pressure is recorded by means of a cannula placed in the venous limb of the capillary loop and the venous pressure is raised by means of a cuff applied to the arm, the capillary pressure rises *pari passu* with the venous pressure, while it falls with normal rapidity to the original level when the pressure on the arm is suddenly released. We have not attempted to repeat this observation, but we would point out that the test may not be free from fallacy, as we found in our case that the skin vessels, including those of the subpapillary venous plexus, dilated readily in response to slight trauma, such as pricking the skin, so that the insertion of a cannula through the skin by causing dilatation might remove any spasm which had previously existed.

Villaret, Saint-Girons, and Grellety-Bosviel,[104]-[106][108] Layani,[61][62] and May and Layani[78] have reported the frequent occurrence of venous hypertension in cases of acrocyanosis; but in our patient the venous pressure as determined by the direct method was entirely normal. There is, therefore, no reason to suppose that the cyanosis is due to distension of the subpapillary venous plexuses and the venous side of the capillary loops as the result of raised venous pressure. The absence of œdema of the dependent parts and of any dilatation of the right side of the heart is also in accord with this finding.

The veins and venules in our case do not appear to present any varicosities, superficial or deep. They are inconspicuous at ordinary room temperatures, although they swell readily when arteriolar dilatation is produced by raising the room temperature or by nerve block (see below). In infra-red photographs the veins of the limbs and abdomen come out prominently (Figure II), but this may be attributed partly to the thinness of the skin and partly to the venosity of the blood.

Capillaries.

All investigators, with the exception of Flarer,[33] who have examined the capillaries under the microscope in acrocyanosis[4][5][29][36][55][58][71][83][85][92]-[110][111] are agreed that they are dilated. The dilatation is most pronounced on the venous side of the capillary loop, which, according to some observers,[55][83][87] may exhibit aneurysmal dilatations, but this is evidently not a constant feature.[71] The vessels of the subpapillary venous plexus are also dilated.

In view of this dilatation of the capillaries and vessels of the subpapillary venous plexus, the question arises as to whether it would suffice to account for all the phenomena of acrocyanosis. As far as the cyanosis is concerned, it would be a contributory factor in determining the depth of the colour, for Lundsgaard and Van Slyke[73] have shown that the amount of reduced hæmoglobin which is necessary to produce cyanosis is influenced by the number, width and length of the blood-filled capillaries per unit area of skin. While Krogh[89] ascribes the colour of the skin chiefly to the state of the capillaries, Danzer and Hooker[28] consider the subpapillary venous plexus to be of greater importance; but it is probable that both of these and possibly to some extent the subpapillary arteriolar plexus influence the colour in varying degrees. The importance of the condition of the vessels as a factor in the genesis of cyanosis, even in the normal subject, is indicated by the observation of Goldschmidt and Light,[35] that when the arm is allowed to hang down and remain stationary, the resulting engorgement of the capillaries and venules is the primary cause of the cyanosis, for the oxygen unsaturation of the blood leaving the part is actually less than when the arm is in the horizontal position. Similarly, Lewis and Landis[71] find that in acrocyanosis the blood flow through the hand is greater when the limb is dependent, although in this position the cyanosis is deeper than when the hand is at the level of the heart. While the depth of the colour is influenced by the number, width and length of the vessels, the tint depends upon the degree of oxygen unsaturation. The intense cyanotic tint in acrocyanosis indicates that the hæmoglobin is becoming abnormally reduced in its passage through the minute vessels. This is borne out by actual determination of the oxygen content of the arterial and venous blood. Whereas in the absence of stasis and at room temperature about 23° C., the arterio-venous oxygen difference in the normal individual at rest is only some six volumes *per centum*, the venous blood remaining about 70% saturated, we have seen that in our patient under the same conditions the arterio-venous oxygen difference in the upper limb was 12·5 volumes *per centum*, the venous blood being only 32% saturated.

The question arises whether the dilatation of the capillaries and venules is alone sufficient to account not only for the cyanosis, but for the increased oxygen desaturation of the blood and the coldness of the extremities. If the total amount of blood passing through the skin remained unchanged, but the capillary bed was greatly widened, there would be stasis in the individual vessels and consequently

a greater oxygen desaturation of the hæmoglobin, with resulting cyanosis. Changes in the state of the minute vessels, apart from any alteration in total blood flow through the part, would therefore go a long way towards explaining the cyanosis, but it is doubtful whether it would be sufficient to account for the degree of cyanosis and oxygen unsaturation actually encountered in our patient.

With regard to the coldness of the hands and feet, it is generally assumed that the temperature of the extremities in relation to the external temperature is an index of the amount of blood passing through the part. If, however, the calibre of the afferent arterioles and the total amount of blood entering the part remained unchanged while the number of blood-filled capillaries increased, there would be greater heat loss owing to the stasis and the increase in the area of the cooling surface. Consequently, the temperature of the part would fall and the limb would feel cold to the touch. It appears, therefore, that dilatation of the capillaries and venules could in large part explain the coldness and cyanosis of the extremities without the assumption that any change in total blood flow occurred; but, as diminished blood flow could also give rise to cyanosis and coldness, it is necessary to find some independent means of determining whether the blood flow is actually unchanged or diminished. The usual method of measuring the blood flow through the hands and feet is that devised by Stewart,[90] which consists in placing the extremity in a water calorimeter and measuring the rate of change in the temperature of the water. Using this method, Lewis and Landis[71] found that in their case of acrocyanosis the rate of rise in the temperature of the water was about half the normal. If the coldness of the limbs had been caused by increased heat loss, without any change in blood flow, the rate of rise in the temperature of the water in the calorimeter should have been greater than normal. This experiment, although only referred to in a footnote in the paper by Lewis and Landis, is, in our view, the most important piece of evidence hitherto brought forward of a diminution in the blood flow in acrocyanosis, and it is desirable that further cases should be investigated by similar means should the opportunity arise.

Some investigators[4][5][92][110] claim to have observed under the microscope the extreme slowness of the movement of corpuscles in the capillaries, but this indicates only the presence of stasis in individual channels and is no proof that the total volume of blood flowing through the part is diminished.

The diminished blood flow and the cooling might conceivably cause a lowering of the metabolism of the tissue, but if any such change in the oxygen consumption does occur, it does not correspond to the diminished blood flow, as the blood loses much more oxygen than normally in its passage through the capillaries.

The diminished blood flow might be due to local causes or to a retardation of the general circulation; but as the available evidence shows that the cardiac output is normal in acrocyanosis,[79] the diminished flow must be due to some obstruction in the peripheral vessels. The evidence already presented regarding the venous outflow indicates that the obstruction is not on the venous side. This is supported by a study of the capillary pressure. If the outflow of blood from the arterioles was unimpeded, but some obstruction to the outflow on the venous side was present, the capillary pressure would rise. Briscoe[8] reported that the capillary pressure, as measured by the pressure necessary to produce blanching, was raised in vasomotor disorders accompanied by cyanosis and also as a result of the application of cold; but Danzer and Hooker[28] have pointed out the fallacies of this method. Using as a criterion of the capillary blood pressure the amount of pressure just necessary to arrest the blood flow through the capillaries as observed microscopically, they found that cold caused a fall, not a rise, in the capillary pressure. Boas,[5] employing this test, found that in acrocyanosis the capillary blood pressure was diminished, while Lewis and Landis,[71] using the direct method, obtained normal values. The evidence therefore points to the conclusion that the obstruction to the blood flow is on the arterial side.

Larger Arteries.

The larger arterial trunks appear to be unaffected in acrocyanosis. No thickening of the vessel walls could be detected on palpation. Radiological examination revealed no calcareous deposits and the superficial pulses were easily palpable in the normal situations. The reactive hyperæmia test, described below, also showed that on the release of the pressure applied to the arm there was no delay in the return of blood to any part of the extremities.

Smaller Arteries.

There is likewise no evidence that the smaller arteries of the order of the digitals are affected. The fingers do not exhibit the blanching characteristic of the Raynaud phenomena, nor do they blanch on exposure to cold, while studies of the increment in the volume of pulsation in the fingers with increasing external temperature[29][71] show that the response of the vessels is normal.

Arterioles, Arterio-Venous Anastomoses, Subpapillary Arteriolar Plexus.

Taking into consideration all the above facts, we arrive by a process of exclusion at the conclusion that the obstruction is in the smaller vessels: the arterioles, the arterio-venous anastomoses or the subpapillary arteriolar plexus; perhaps all three.

It is now necessary to try to account for the two changes which have been shown to be present, namely, arteriolar obstruction and capillary dilatation. The attempt to do so raises two important issues: (i) Can the changes be referred primarily to the capillaries or to the arterioles, or are both capillaries and arterioles affected simultaneously but independently by a common factor? (ii) Is the condition of the vessels due to functional or to structural changes?

Seat of the Primary Change.

We have seen that dilatation of the capillaries would account for many of the phenomena of acrocyanosis, such as cyanosis and even coldness; but if all the changes in acrocyanosis were primarily due to capillary dilatation, as has been supposed by May and Layani,[78] it would be necessary to show that the arteriolar obstruction could also be an indirect result of this dilatation. It is conceivable, for example, that arteriolar constriction, and therefore diminished blood flow, might be a local effect of cooling resulting, as already explained, from capillary dilatation. Briefly, the issue is whether the cooling is due to arteriolar obstruction or whether arteriolar contraction is the result of cooling. The most important piece of evidence bearing on this point comes from the experiment on the determination of the blood flow with Stewart's calorimeter. An essential part of the technique of this experiment is the preliminary immersion of the extremity in a water bath at approximately the temperature of the water in the calorimeter for a period of ten minutes or more, so that the temperature of the part may be rendered uniform and all observations can start at the same temperature. As this preliminary warming of the hands for an adequate length of time would be of especial importance in acrocyanosis, it is a pity that no details are given of the recorded experiments; but if we assume that sufficient attention was paid to this point, the results of Lewis and Landis would indicate that even after the hands of the patient with acrocyanosis had been brought to the same initial temperature as those of a normal control, the subsequent record with the calorimeter gives evidence of a diminished blood flow. It is evident from this observation that arteriolar constriction, if present, cannot be due to a cooling effect, since it persisted after the hands had been warmed. The hypothesis that we are dealing with arteriolar constriction secondary to the capillary dilatation is therefore untenable.

As to the reverse possibility, namely, that the capillary dilatation is secondary to the arteriolar obstruction, we know from the work of Lewis[67] and his collaborators that oxygen lack and stasis cause the production and local accumulation of histamine-like bodies which cause capillary dilatation. It is difficult, however, to assess the exact importance of this factor in acrocyanosis, for H-substance dilates the arterioles as well as the capillaries, and, as the experiments described below demonstrate, the arterioles readily react to histamine and to mechanical stimulation in acrocyanosis. It would be necessary to suppose that the amount of H-substance present in the tissues was sufficient to cause dilatation of the capillaries, but yet insufficient to cause relaxation of the arterioles, otherwise the arteriolar spasm would be abolished and the skin would become red. There is also a lack of the characteristic sensation caused by the concentration of histamine in the skin, but this may perhaps be explained by the absence of whealing, owing to the development of the refractory state (see below). Krogh[59] and his co-workers have shown that oxygen lack and increased carbon dioxide tension can cause relaxation of the capillaries and opening up of the capillary bed quite apart from stasis, and it is possible that the loss of capillary tone in acrocyanosis may be in part, if not entirely, due to the direct effect of chronic oxygen lack and increased carbon dioxide tension upon the capillary walls. Krogh[59] and Rehberg found that arterial anoxæmia produced by breathing atmospheres deficient in oxygen causes dilatation of the arterioles as well as of the capillaries in the rabbit's ear. In acrocyanosis there is no arterial anoxæmia to cause relaxation of the arterioles, but the low oxygen tension develops distal to the arterioles, more particularly in the venous end of the capillaries, and it is precisely here that the dilatation is most pronounced.

Whatever may be the nature of the substances causing vaso-dilatation, it is clear that narrowing of the arterioles can lead to chemical changes which result in capillary dilatation.

Character of the Vascular Changes.

Are the vascular changes structural or functional? In order to answer this question it is necessary to examine the reaction of the vessels to various stimuli.

Capacity to Dilate.

Response to Heating the Whole Body.—The response to heating the whole body was estimated in our case.

The patient was placed in a chamber which could be heated up to any desired temperature, and skin temperatures were taken at intervals. The results are set forth in Tables I and II, while Figure IX shows simultaneous

TABLE I.

Experiments in Hot Room. Experiment Number 1.

Time. p.m.	Room Temperatures in Degrees Fahrenheit.	Skin Temperatures in Degrees Fahrenheit.		Comment.	
		Foot (Dorsum).	Hand. (Dorsum).	Foot.	Hand.
3.40	68	72	76	Cyanotic.	Cyanotic.
3.45	73	73	77	Cyanotic.	Cyanotic.
3.55	76	75	78	Cyanotic.	Hands pinkish.
4.0	78	75	78	Feet still dusky, cyanotic.	Hands pink, veins engorged.
4.5	80	77	79	Feet still dusky, cyanotic.	Hands red, hot, clammy, veins engorged.
4.15	81	78	86	Feet still dusky, cyanotic.	Hands red, hot, clammy, veins engorged.
4.20	82	81	92	Feet still cyanotic, lower leg flushed.	Hands red, hot, clammy, veins engorged.
4.30	84	81	92	Feet still cyanotic, lower leg flushed.	Hands red, hot, clammy, veins engorged.
4.40	86	82	92·5	Feet less dusky, clammy, veins visible.	Hands red, hot, clammy, veins engorged.

TABLE II.

Experiments in Hot Room. Experiment Number 2.

Time.	Room Temperatures in Degrees Fahrenheit.	Skin Temperatures in Degrees Fahrenheit.			Comment.	
		Foot (Dorsum).	Hand (Dorsum).		Foot.	Hand.
			Patient.	Control.		
a.m. 11.0	63	67	76	79		
11.10	77	72	78·5	79		
11.20	79	73	79	84		
11.25	81	75	81	84		
11.30	82	75	81	86	Feet cold, cyanotic.	Hands pinkish.
11.35	84	75	82	86		
11.40	87	78·5	88	91	Feet less cyanotic.	Hands pink, warm, veins engorged.
11.50	90	79	92	91	Feet moist.	Hands clammy.
p.m. 12.10	91	80	92	89		(Control sweating freely.)

records of the skin temperature on the dorsum of the hand in the patient with acrocyanosis and in a normal control. It will be observed that in the patient the temperature of the skin is lower throughout the greater part of the experiment and that there is a delay in the onset of the sharp rise in temperature indicative of vaso-dilatation. Once the temperature does begin to rise, however, it goes up rapidly and ultimately reaches as great a height as in the control. The slight fall in the temperature of the skin when the room temperature approached 90° F. is accounted for by evaporation caused by sweating. When the temperature of the room reached 87° F. and that of the skin of the hand 88° F. in the second experiment, the cyanosis of the hand completely disappeared and was replaced by a bright pink colour, while the veins which had previously been collapsed stood out prominently. The temperature of the feet remained from 5° to 10° F. below that of the hands throughout the experiment; and although the feet became less cyanotic, they never became pink. There was also in both experiments an absence of any sharp rise of temperature in the feet. In the first experiment the significant rise of the skin temperature in the hands was sharper and took place at a lower room temperature than in the second experiment.

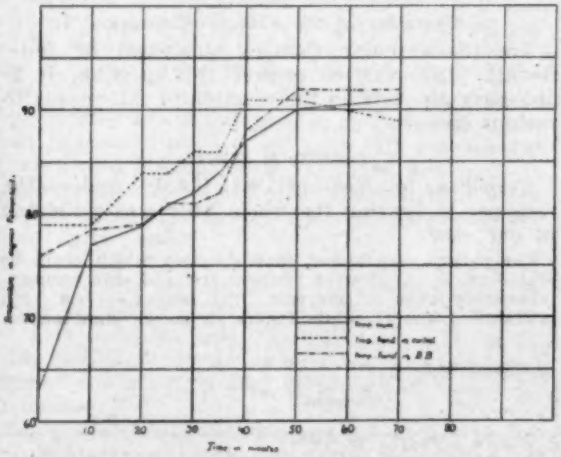

FIGURE IX.

Graph of skin temperature of patient with acrocyanosis and of normal control with progressive rise in room temperature.

This may have been due to the higher initial temperature of the room and the slower rate of heating, both of which would allow the more thorough heating up of the blood and of the hand, *pari passu* with the rise of room temperature. Hence the vasomotor tone would be relaxed before the temperature of the room had risen to the same point as in the second experiment. It would have been desirable to obtain the rectal temperature of the subjects, but this had to be omitted. This experiment shows that the vessels can relax completely in response to heating and therefore that there is no structural change in the vessel walls to account for the arteriolar obstruction to the blood flow. The retardation in the rise of temperature suggests that there is greater difficulty in bringing about arteriolar dilatation in acrocyanosis than in the normal subject. On the other hand, it might be due to the fact that the hand of the patient with acrocyanosis is colder to begin with and takes a longer time to heat up. Lewis and Pickering[73] have drawn attention to the fact that when the limbs are initially at different temperatures their responses are not simultaneous, there being a delay in vaso-dilatation in the colder limb. In the second experiment, however, there was a delay in the rise of temperature even after the skin temperature had reached or exceeded the point at which the sharp rise occurred in the control; but it is uncertain to

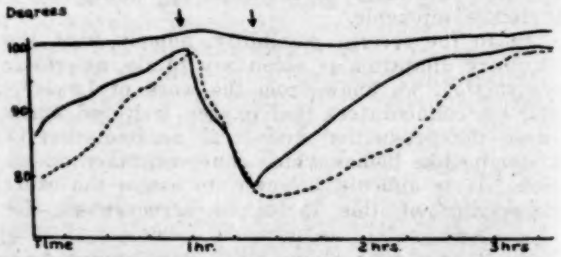

FIGURE X.

Temperature curves. The top line shows the rectal temperature of a monkey, the lower continuous line the temperature of the normal left foot, and the lower broken line the temperature of the right foot after extirpation of the left premotor area and of the cortex. At the point indicated by the first arrow the animal was removed from the 90° F. temperature of an incubator to an environmental temperature of 45° F.; at the point indicated by the second arrow the animal was replaced in the incubator.

what extent the deeper structures had ben warmed. The experiment, therefore, does not decide conclusively whether the coldness of the limb and the lag in the rise of temperature are the result of vascular spasm or the converse. On the other hand,

the fact that the response is delayed, even when the heating up process is very slow (two hours), as in an experiment reported by Lewis and Landis,[71] rather points to the first alternative. What is really required in order to settle the question is a comparative record of the vasomotor responses of patients with acrocyanosis and normal controls when the blood (rectal) temperatures and the room temperatures are at corresponding levels.

Response to Heating the Trunk or Two Extremities Alone.—Elliott, Evans and Stone[29] heated their subject's body in a cabinet and recorded the skin temperatures of the exposed limbs. Alternatively they immersed two of the patient's limbs in hot water, as described by Landis and Gibbon,[60] and recorded the skin temperatures of the other limbs. This method of producing vaso-dilatation acts by raising the temperature of the blood.[60][102] The results obtained correspond to those recorded in the above experiments, namely, a slightly delayed response and lower skin temperatures in the patient with acrocyanosis as compared with a normal control, but ultimately complete relaxation of the skin vessels in both. Unfortunately, the rectal temperature was not taken, and, although the mouth temperature was taken, the figures are not recorded.

Reactive Hyperæmia.—The reactive hyperæmia of our patient was estimated.

The right hand of the patient was immersed in water at a temperature of 110° F. for ten minutes. The cyanosis disappeared and the hands became bright pink in colour. The right hand was then held in the vertical position for two minutes when it became blanched. With the hand still elevated, a manometer cuff was placed on the upper arm and the pressure was raised to 200 millimetres of mercury. On lowering the hand to the horizonal, it remained blanched, even when it was again immersed in a water bath of 110° F. The pressure in the cuff was then released suddenly and within seven seconds the hand again became completely flushed.

Lewis (1936)[74] gives two to five seconds as the normal time, so that the delay in our patient was slight and of doubtful significance. It could be accounted for either by a slight increase in arteriolar tone, or by the greater length of time required to fill the relaxed capillaries. At all events, there is no doubt about the ability of the vessels to relax.

Nerve Block.—A nerve block experiment was carried out in our patient.

Nerve block was produced by injecting five cubic centimetres of 2% "Procaine" solution into the ulnar nerve on the posterior aspect of the medial epicondyle of the humerus and into the posterior tibial nerve below the internal malleolus of the tibia. The results are set forth in Tables III and IV and illustrated in Figure XI.

These experiments show that when the vaso-constrictor nerves are paralysed, complete vaso-dilatation takes place. Cyanosis disappears entirely, the paralysed part becomes warm and bright pink in colour, while the veins stand out prominently. As the capillaries are already relaxed, the pinkness cannot be explained by capillary dilatation alone. It must, therefore, be due to removal of stasis and the increased filling of the capillaries resulting from relaxation of anteriolar spasm. The previous dilatation of the capillaries and enlargement of the capillary bed are probably the cause of the bright pink colour.

Lewis and Landis,[71] in a similar experiment, observed that the rise of temperature occurred before the change of colour, and they suggest that the rise of temperature is due to primary relaxation of the deeper vessels or of the arterio-venous anastomoses, and that there is a failure of the cutaneous arterioles to relax until they are warmed. The delay in the increase of blood flow through the cutaneous vessels is adduced as evidence that the original spasm of the cutaneous vessels was not of nervous but of local origin. Elliott, Evans and Stone[29] recorded similar findings. We are unable to confirm these observations in the present case. In our patient the colour change was observed before the rise of temperature and therefore could not have been caused by it.

Grant and Bland,[37] in their work on anterio-venous anastomoses, draw attention to the lack of correspondence between capillary blood flow and temperature change. The fact that there is no constant relation between the blood flow through the superficial and the deeper vessels, and that the temperature is largely dependent upon the latter, indicates that there is nothing inconsistent between our findings and those of the observers just cited. On the other hand, we cannot regard the greater

TABLE III.

Foot. Posterior Tibial Nerve Block.

Time.	Room Temperature in Degrees Fahrenheit.	Skin Temperature in Degrees Fahrenheit.			Comment.
		Sole, Toes, Sides.	Dorsum, Third Cuneiform.	Upper Half of Leg.	
a.m. 10.45	70	71	72	78	Temperature gradient before injection.
11.0	4·5 cubic centimetres of procain injected 2 centimetres below medial malleolus.				
11.15	70	71	72	78	Slight flush on medial side; no temperature changes.
11.30	70	74	72	78	Flush extended to toes.
11.40	70	76	72	78	Flush extended to toes.
11.50	70	79	74	78	Flush extended to toes.
12.0	70	88	82	78	Sole, medial, lateral, toes flushed and warm.
p.m. 12.30	70	90	88	78	
2.0	70	82	75	78	

TABLE IV.

Hand. Ulnar Nerve Block.

Time.	Room Temperature in Degrees Fahrenheit.	Skin Temperature in Degrees Fahrenheit.				Comment.
		Ulnar Side of Hand, Dorsum, Palm.	Little Finger, Ulnar Side of Ring Finger.	Radial Side of Ring Finger, Middle and Index Fingers.	Radial Side of Hand.	
a.m. 10.20	70	74	72	72	74	Skin temperature before injection.
10.40	Injection of 5 cubic centimetres of procain, posterior aspect of medial epicondyle.					
10.50	70	74	72	72	74	Flushing over ulnar distribution, no temperature change.
11.5	70	80	80	72	74	
11.15	70	82	85	72	74	Veins prominent over dorsum.
11.30	70	82	85	72	74	
11.40	70	78	81	72	73	Elevation of hand for five minutes. Little finger became 4° colder.
p.m. 12.10	70	84	86	72	74	Note rise of 10° to 14° F. over ulnar distribution.

refractoriness of the superficial arterioles as a constant feature of acrocyanosis, and therefore we do not consider that the experiment affords evidence that the change is of local origin and not due to a disturbance of innervation. In the experiment in which the ulnar nerve was paralysed, the pink area corresponded exactly with the distribution of the sensory fibres of the ulnar nerve in which the vasomotor fibres run,[68][69][101][112] and, except over a small area on the dorsum of the hand, there was a sharp line of demarcation between the pink and the cyanosed areas. Had the dilatation of the superficial vessels been dependent upon a heating effect from the deeper tissues, it seems likely that it would have spread beyond the confines of the distribution of the ulnar nerve. The rise of temperature and the change of colour cannot be attributed entirely to increased blood flow through the arterio-venous anastomoses, since the distribution of these anastomoses is limited, while the colour change was observed over parts where the anastomoses are few or absent; for example, over the dorsal surface of the phalanges.[37]

Response to Acetylcholine.—Since acetylcholine has been shown in animal experiments[23][24] to cause dilatation of the arterioles, not only of the splanchnic area, but also of the limbs, it might at first seem that it would be a valuable physiological reagent for testing the vasomotor reactions in acrocyanosis.

Acetylcholine hydrobromide was injected intramuscularly in doses of 0·15 gramme and the temperature changes over the cyanotic areas were recorded. So far as the limbs are concerned, the results were entirely negative. There was a slight rise of temperature in the face, beginning within five minutes of the injection and persisting for forty minutes. The long duration of the dilatation of the vessels of the face suggest that it may have been partly emotional in origin (see Table V).

In another experiment, eserine, which intensifies the vascular effects of acetylcholine,[44] owing to its inhibiting the hydrolysis of acetylchlorine[39] by esterase,[77] was injected subcutaneously in doses of 0·6 milligramme (one one-hundredth of a grain) twenty minutes before the injection of acetylcholine, but again there was no change in the temperature of the limbs.

These negative results are not to be interpreted as demonstrating an increased refractoriness of the arterioles to acetylcholine in acrocyanosis, nor do they prove that the arterioles are unaffected, as Villaret, Justin-Besançon and Cachera[106] on the basis of similar observations have supposed, for it has been shown that even in normal subjects the administration of acetylcholine subcutaneously or intramuscularly in doses as large as 0·5 gramme has no appreciable effect.[10] It has also been found that the administration of the more potent drug acetyl-β-methylcholine subcutaneously to normal[95] or to hypertensive subjects[85] in doses (up to 25 milligrammes) sufficient to produce pronounced vaso-dilatation in the skin of the face and neck, sweating, salivation and fall of blood-pressure, does not cause any rise in the skin temperature of the hands and feet nor any increase in blood flow through the extremities as determined by Stewart's method.

TABLE V.

Acetyl-choline Hydrobromide 0·15 Gramme Intramuscularly.

Time.	Room Temperature in Degrees Fahrenheit.	Skin Temperature in Degrees Fahrenheit.				
		Face.	Hand.	Fingers.	Foot.	Toes.
		Control 86	Control 80	Control 76	Control 74	Control 70
p.m. 12.5	70	88	78	74	73	70
12.10	Injection of acetyl-choline hydrobromide.					
12.25	70	90	79	76	73	70
12.35	70	90·2	79·2	76	73	70
12.40	70	91	79	76	73	70
12.50	70	91	79	76	73	70
12.57	70	89	79	76	73	70

Owing to the ease with which acetylcholine undergoes hydrolysis and the frequency with which inactive commercial preparations are met with, it is necessary to exercise caution in drawing conclusions from some of the published records of its action. We took the precaution of employing acetylcholine bromide which had been freshly recrystallized from alcohol, and our results are in agreement with those obtained by the use of acetyl-β-methylcoline, namely, dilatation of the vessels of

the blushing area without any appreciable effect upon the vessels of the extremities.

Response to Histamine.—Dale and Richards[24] have shown that, whereas the site of action of acetylcholine is the arterioles, histamine acts chiefly upon the capillaries. In man, however, histamine causes dilatation of the arterioles as well as of the capillaries.

Injection of one milligramme of histamine phosphate intramuscularly was followed in our patient by flushing of the hands and feet, unaccompanied by any rise of skin temperature. On the other hand, the face, limbs and conjunctivæ became pallid and the patient felt faint.

These results show that when dilatation of the superficial arterioles was produced the cyanosis was abolished. The dilator action upon the capillaries could not have been responsible for the colour change, as the capillaries are already dilated in acrocyanosis. The absence of any rise of temperature and the appearance of the symptoms and signs of incipient syncope may have been due to the diversion of blood to the internal organs and muscles or to a toxic action upon the heart.

When histamine is injected into the skin it normally calls forth the "triple response".[67] It was, therefore, of interest to study the reaction of the vessels to histamine in acrocyanosis.

Histamine was pricked into the skin over the cyanotic areas on the dorsum of the foot and hand, and, as a control, a similar test was carried out on the non-cyanotic skin of the thigh and upper arm. Over the normal skin the usual response (red reaction, wheal and flare) was obtained, the wheal being well marked. Over the cyanotic area there was no trace of a wheal, but a bright red reaction appeared at the point of injection and was soon followed by a rapidly spreading flare (see Figure XII). The flare was of a much brighter red colour than that over the normal skin; it was also more extensive and persisted longer, while its outline was more irregular.

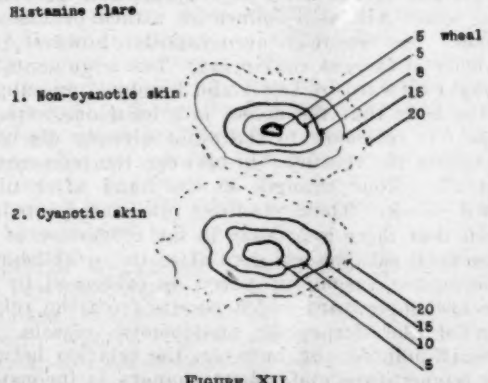

FIGURE XII.
Histamine flare in non-cyanotic skin and in cyanotic skin. The figures refer to the number of minutes elapsing from the time of injection.

We have not followed the skin temperature changes during the development of the flare, but Lewis and Landis[71] state that the rise of temperature is greater in acrocyanosis than in the normal. This finding could not be corroborated by Elliott, Evans and Stone.[29] It is evident, however, that the arterioles react promptly and fully to the injection of histamine in the doses employed; and once they have relaxed, the cyanosis disappears. The test provided further evidence that there is no structural change in the arterioles; but without quantitative observations it would be impossible to say whether they are more refractory to histamine than the normal vessels. The irregularity and greater extent of the flare could be accounted for by the relaxed state of the capillaries and of the venules of the subpapillary venous plexus; its persistence could be attributed to stasis. It may be mentioned in passing that it is difficult to compare the outline of the flare over the normal with that over the cyanotic area, because the colour contrast renders it much easier to define the limits of the flare on the cyanotic background.

Response to Mechanical Stimuli.—An attempt was likewise made to elicit the triple response by means of stroking the skin firmly with the blunt end of a pencil.

As in the preceding observations, the skin was tested over the cyanotic areas on the back of the hand and foot and over the normal skin of the thigh and upper arm. The responses were similar to those obtained with histamine. A red reaction followed by a well-marked wheal appeared on the arm and thigh, but no wheal was produced on the hand and foot. The flare over the cyanotic areas was again more extensive and irregular in outline than over the normal skin and it also persisted longer. It was likewise of the characteristic vivid red colour.

Permeability of the Capillaries.

Since the production of a wheal is held[67] to be due to increased permeability of the capillary walls resulting from the action upon them of histamine or H-substance, the absence of whealing indicates that some change has taken place in the capillary walls rendering them irresponsive to stimuli in so far as changes in permeability are concerned. This is in marked contrast to the prompt response in respect of local dilatation and reflex flare. The observation affords further evidence that the production of the flare, which is dependent upon an axone reflex and the development of the wheal which results from a direct chemical stimulus to the vessel wall, are independent events. The failure to wheal in acrocyanosis is similar to the condition of "refractoriness", described by Lewis and Grant.[66] This state can be produced by cooling the part or by previously puncturing the skin with histamine. In acrocyanosis the extremities are indeed cold, but no wheal appears even when the parts are flushed and warm. It is possible that the refractoriness may be due to the prolonged effect of the local accumulation of histamine resulting from vascular stasis. In view, however, of the prompt vaso-dilatation which occurs when histamine is injected, it would appear probable that if local accumulation of histamine had been a factor, it would have given rise to dilatation of the arterioles with consequent abolition of the cyanosis. Alternatively, it would be necessary to suppose that the local concentration of histamine was just sufficient to induce the refractory state, but yet insufficient to cause vaso-dilatation, which seems a straining of hypothesis. Whether chronic anoxæmia without stasis is capable of inducing the refractory state is unknown, but it is a possibility that requires to be tested.

Capacity to Contract.

Response to Adrenaline.—Adrenaline acts chiefly upon the arterioles, causing vaso-constriction, but, in the case of the human skin, it also causes some constriction of capillaries and venules. Thus Cotton, Slade and Lewis[28] have found that when pricked into the skin, it causes blanching, even after the arrest of the circulation through the limbs. The constriction of the minute vessels has also been observed microscopically.[11][40] The action is obtained even after the degeneration of nerves and is due to a direct action upon the vessel walls.[7][68]

Adrenaline solution (1 in 1,000) was pricked into the skin in the usual manner, the areas selected being the same as those in the preceding experiments. Over the non-cyanotic areas the blanched area attained its maximum size (eight millimetres) in ten minutes and it had decreased slightly at the end of twenty-five minutes. Over the cyanotic areas the skin became blanched equally rapidly, the blanched area also attaining its maximum size in ten minutes, although it was of greater size (14 millimetres). At the end of twenty-five minutes the blanching had become diffuse and its outline ill-defined.

These results show that the vessels are capable of responding to adrenaline by contraction. The greater size and irregularity of the blanched area over the cyanotic parts could be explained by the spread of the adrenaline in the skin due to the larger number of open and relaxed capillaries.

Response to Pituitrin (Vasopressin).—Vasopressin acts almost exclusively upon the capillaries in the human subject. When pricked into the skin of the upper arm and thigh, it produced a pale area of about four millimetres in diameter, which attained its maximum size in about ten minutes and persisted unchanged for about twenty-five minutes. Over the cyanotic parts it also produced a pale area of about the same size, but the pallor was not quite so pronounced as over the normal skin.

The most striking demonstration of the effects of vasopressin on the capillaries was obtained by intramuscular injection of the drug. The results are illustrated in the colour plates.

One cubic centimetre of pituitrin was injected intramuscularly into the patient and a similar dose into two normal controls, and in each case the subject was photographed (see Figures III, IV, V and VI) twenty minutes later. Both the normal subjects had pink cheeks at the temperature of the room. After the injection, the skin of the face and extremities became intensely and uniformly pale, with the exception of a very small area in the centre of the cheek of one of the controls (female). The patient also exhibited marked pallor, but the blanching of the extremities was more patchy, and, although there was a general pallor of the face, there still remained a definite trace of cyanosis over a small area in the centre of the cheeks. The injection of 0·5 cubic centimetre of pituitrin yielded similar results, only less marked.

This experiment demonstrates that the capillaries are still capable of contraction and that the disease does not involve a structural change in the capillaries, analogous, say, to relaxed and varicose veins. The tonus of some of the capillaries and small venules of the subpapillary plexus, for example, those of the middle of the cheek, has, however, been so far lost as to render the vessels somewhat less reactive.

Underlying Cause of the Vascular Changes.

We have seen from the preceding section that the balance of evidence points to the conclusion that the essential vascular change consists in the functional spasm of the terminals of arterioles, as Lewis and Landis[71] have suggested. At the same time the capillaries and the minute vessels of the subpapillary venous plexus are dilated. It is now necessary to discuss the underlying cause of these changes and whether they are to be ascribed to local, remote or general factors.

Secondary Ætiology: the Factors Controlling Vasomotor Tone.

Local Factors.—As regards possible local causes, the fault may be in the vessels themselves, or the condition may be due to abnormal chemical changes in the tissues. Among the normal reactions of the tissues to cold of a certain intensity is the production of H-substance.[70] If the change in acrocyanosis consisted in an exaggeration of the local response to cold with excessive production of H-substance, there would be dilatation, not only of the capillaries, but also of the arterioles, and the hands would be red instead of blue, as they are in the normal reaction to super-cooling.

Lewis[74] maintains that both in Raynaud's disease and in acrocyanosis the fault lies in the vessels themselves and that the condition is not due to a disturbance of vasomotor innervation. In Raynaud's disease this is shown by the fact that even after vasomotor tone has been reduced either by warming the body or by nerve block, the immersion of the hand of a susceptible person in cold water will still induce an attack of vascular spasm. As regards acrocyanosis, however, the evidence is far less convincing. Two arguments are brought forward by Lewis and Landis[71] in support of the view that the defect is a local one. One of these has reference to the point already discussed regarding the relationship between the temperature and the colour changes in the hand after ulnar nerve block. Their findings are interpreted to mean that there is a delay in the relaxation of the superficial skin vessels even after the establishment of complete vasomotor palsy, as evidenced by the rise of temperature which results from the relaxation of the deeper or anastomotic vessels. As already pointed out, however, the relation between the temperature and colour changes is inconstant. Our own observations might with equal justification have been interpreted to mean that the chief delay in relaxation is in the deeper and anastomotic vessels, which may very well have been the case in this particular patient. Lewis and Landis[71] also stress the fact that the colour change after nerve block is very gradual and not abrupt as it is in Raynaud's disease following the release of vasomotor spasm. We would point out, however, that the site of the vascular spasm in acrocyanosis is more distal, and the vessels would relax only by

degrees at various points as the corresponding vasomotor fibres became progressively blocked with the penetration of the anæsthetic into the nerve trunk, whereas in Raynaud's disease relaxation of the spasm of one of the larger vessels of the order of the digital arteries would immediately allow blood to enter simultaneously the capillaries in the distribution of that vessel.

The second argument is that when the hand was immersed in water at 17° C. after complete vasomotor paralysis, the colour of the anæsthetized area, although pinker than the rest of the hand, was still cyanotic. At this temperature, however, the arterioles would begin to contract owing to the direct action of cold upon them, and the resulting stasis of blood in the relaxed and hypotonic capillaries and venules would account for the relative ease with which the bluish colour returned. Elliott, Evans and Stone[29] have compared the reactions of the normal finger with that of the finger of the patient with acrocyanosis after nerve block. They report that when the anæsthetized finger of the patient was immersed in water at 15° C. it took on a slight but definite blueness; but on the removal of the finger from cold water the skin temperature response was precisely the same as in the normal anæsthetized finger. On the other hand, the rise of temperature of the unanæsthetized fingers of the acrocyanotic patient was very much less than that of the unanæsthetized fingers of the normal individual. This experiment shows that the effect of nerve block is to cause the fingers in acrocyanosis to behave in precisely the same manner as the normal anæsthetized finger in respect of the response to changes in external temperature as measured by the skin temperature changes. If the defect was a local one, independent of the action of vasomotor nerves, some delay in response might have been anticipated, a delay similar to that observed when the nerve supply is intact, as in the unanæsthetized area, or when the vasomotor tone is diminished as a result of heating the body. The only difference, and that is a slight one, is in the colour change, and this can probably be accounted for by the condition of the capillaries and the venules of the subpapillary plexus which remain in an abnormal state of relaxation.

Rôle of the Nervous System.—While a study of the vascular responses fails to provide satisfactory evidence that the defect is a local one, there are certain general considerations which militate against this conception. The diffuseness, symmetry and permanence of the cyanosis, the frequency with which it is associated with disturbances of growth and metabolism, the fact that it has been known to develop with comparative rapidity, and that it has been reported as a sequela of encephalitis, all point to its being due either to some general disturbance of metabolism or to a defect in the central mechanism controlling the tone of the vessels of the extremities and face.

The coincidence between the distribution of the cyanosis and that of the autonomic nerves to the vessels of the limbs is very suggestive. Woollard and Weddell[118] find that there is a tendency for the non-medullated (vaso-constrictor?) fibres to increase as the distal part of the limb is reached.

The facts that there is no general rise of blood-pressure and that the vascular change is confined to the exposed parts from which heat loss is greatest, and more particularly the distal portions of the extremities, suggest that the defect lies in the central control of the vascular mechanism concerned either with the regulation of body temperature or with the adaptation of vasomotor tone to posture. The same reasons render it improbable that the primary change is in the vasomotor centre in the medulla. Since the distribution of the cyanosis does not correspond to that of the nerve supply through any particular peripheral nerve or spinal segment or sympathetic ganglion, it is improbable that the disturbance arises at any of these levels.

A study of the skin temperatures shows that the subject of acrocyanosis has a very steep vasomotor gradient in the limbs, and this appears to be an important feature of the disorder. Together with the peculiar distribution of the vascular changes, it raises the question as to the functional relationship between parts of the brain and the vasomotor control of the face and extremities. It has long been known[12][36] that lesions of the motor area or of the internal capsule may be accompanied by vasomotor changes in the contralateral limbs. In man these changes appear to be irregular. In some cases the affected extremity is colder, in others warmer than its fellow, while it is not uncommon to find the condition of coldness alternating with that of warmth. The vascular response to heating and cooling of the body is frequently normal.[103] Stewart[90] found that the blood flow through the cold extremities in hemiplegia was diminished. These varying effects may be due to the lesions being partly irritative and partly destructive, or possibly to the involvement in varying degree of two different sets of fibres, one vaso-dilator and the other vaso-constrictor. But the existence of two distinct sets of cortical fibres having these functions has not been definitely proved. Eulenberg and Landois,[32] in experiments on cats and dogs, have shown that stimulation of the cortex in the neighbourhood of the motor area gives rise to temperature changes in the contralateral limbs. Recent experimental and clinical evidence[34][53] indicates that the premotor area is concerned with the vasomotor control of the limbs, face and ears. Kennard[54] has found that ablation of the premotor cortex on one side in monkeys is regularly followed by coldness of the extremities on the contralateral side. The coldness is not due to sweating, as there was actually a diminution in sweating in the affected limbs. It is also not due to motor-paralysis, as it persisted after all motor disturbance had disappeared. The temperature of the skin, face and ears, as well as of the palm and sole, is affected. When the animal was put into a refrigerator, the skin temperature in

the affected and unaffected extremities fell equally and simultaneously, but on transference from the refrigerator to an incubator at 90° F. there was a delay in the rise of temperature of the affected limb, although ultimately the temperature on the affected side rose to that of the normal side. The curves of skin temperature obtained from the normal and affected limbs (see Figure X) during the heating process exhibit differences very similar to those already described in the experiment on heating the whole body of the normal person and of the patient with acrocyanosis (compare Figure IX). In both there is a lag in the rise of temperature in the affected limbs, but ultimately the limbs attain the same temperature, showing that the vessels can dilate fully. The experiment shows that a type of vasomotor reaction closely resembling that found in acrocyanosis can result from a lesion of the central nervous system. It is not certain whether the vaso-constriction is a release phenomenon, due to removal of inhibition, or whether it is due to the cutting off of tonic impulses to the vaso-dilator mechanism. The vaso-dilator impulses which pass out by the posterior roots are evidently not involved, as the effect is obtained after deafferentation of the cord. The efferent vaso-constrictor impulses must therefore pass out by the anterior roots.

The most important feature of our case which would suggest a possible cortical origin of the acrocyanosis is the existence of mental deficiency. Apart from the vasomotor disturbance, however, there was none of the characteristic signs of a premotor cortex lesion, such as forced grasping, spasticity and impairment of skilled movements. If the disorder has anything to do with the premotor cortex, it must be selective as regards the neurones subserving vasomotor tone and it must be bilateral. The question arises as to whether a cortical defect could explain the abnormalities of growth and metabolism which were present in our patient. The relationship between cortical defect and impaired growth and metabolism is obscure. Perhaps it has to do with involvement of the connexions between the cortex and the hypothalamus (see below), which is concerned with the control of vegetative and metabolic functions. At all events, it is well known that many degenerative cerebral affections of early development (porencephaly) may be associated with sexual dystrophy. It is noteworthy that in our patient we are evidently dealing with a type of sexual dystrophy which differs in some respects from that commonly associated with glandular insufficiency, for the epiphyseal junctions are closed and the bone age is normal.

As bearing upon the hypothesis of a cortical origin of the mental and vasomotor changes, the frequency with which cyanosis and coldness of the extremities is met with in the catatonic form of *dementia præcox*[16][57] should be mentioned. Crocq,[19][20][21] Cassirer[12] and Comby[17] have also remarked on the mental instability of their patients with acrocyanosis.

It seems clear that neither mental defect nor impairment of development is a constant feature of acrocyanosis, but it would be unjustifiable to dismiss the association between them as entirely fortuitous. The case under consideration and the evidence just discussed point to the possibility that some forms of acrocyanosis may be due to a cortical defect, and that this defect—degeneration, abiotrophy, functional insufficiency or whatever it may be—may in some cases be more or less limited to the neurones of the premotor cortex subserving vasomotor tone, while in others the defect may also involve other parts of the cortex; for example, the adjacent portion of the frontal lobes.

A considerable body of evidence exists to show that certain nuclei of the diencephalon, more particularly those of the *tuber cinereum*, have to do with the regulation of body temperature and with vasomotor tone. Electrical stimulation of lesions of this region[3][26][47][48][49][50][52][63][93] give rise to changes of body temperature, either hypothermia or hyperthermia, accompanied by vasomotor changes. Warming up the blood going to this part of the brain causes dilatation of the skin vessels, and cooling it causes vaso-constriction.[2] The possibility therefore exists that some cases of acrocyanosis may be due to a disturbance of the function of these centres. Encephalitis, which is prone to attack this part of the brain, is reported to have been followed by acrocyanosis,[78][81][100] but, of course, it may also effect the cerebral cortex. The same perhaps applies to *dementia præcox*, which, according to some authors,[16] may affect both the cortex and the basal ganglia, but some uncertainty exists regarding the histological findings in this disease. That a disturbance of part of the heat-reacting mechanism, namely, that concerned with the regulation of heat loss and the blood flow through the vessels of the skin, may be a cause of acrocyanosis is suggested by the marked changes in the circulation through the skin of the extremities, which follow cooling of the blood or which result from the action of toxins upon the heat-regulating centres—changes which are unaccompanied by any significant rise in the general blood-pressure. The cold and blue extremities which may be observed during the stage of rigor in some fevers and which are perhaps best seen in the cold stage of a malarial paroxysm, present a picture having some resemblance to acrocyanosis, and Stewart[97] has shown that in such conditions the blood flow through the hand is diminished. Hunt[43] has shown that when the temperature of the body is lowered to between 95° and 96° F. (rectal temperature) in man by immersing the body in cold water, the extremities, cheeks and ears become blue; later, pallor and Raynaud phenomena appear. Here the changes which occur in the peripheral vessels are not quite the same as in acrocyanosis, since contraction of the larger arteries evidently occurs as evidenced by blanching. This may be due to the fact that the cold blood acts not only upon the central mechanism, but may also have a direct action upon the smaller arteries. The coldness and blueness of the extremities seen in fever occur under conditions more closely resembling those in acrocyanosis, in that the temperature of the blood reach-

ing the peripheral vessels is not lowered and blanching of the fingers is not such a prominent feature. It is conceivable that in some forms of acrocyanosis there is a functional disorder of the hypothalamic centres controlling the circulation through the skin of the extremities, the centres behaving, as they do in fever, as though they were reacting to cold, even although the external temperature is not lowered and the temperature of the blood remains normal.

The occurrence of sexual dystrophy and changes in sugar tolerance would fit in with the hypothesis of a diencephalic origin of acrocyanosis, but in this connexion the functions of the hypothalamic nuclei cannot be considered apart from the pituitary gland.

Endocrine and Neuro-Endocrine Factors. — Among some of the earlier cases of what may have been acrocyanosis described in the literature are some in which the condition is reported to have occurred in association with pituitary syndromes, such as acromegaly.[6][42][94] We have also observed cyanosis and coldness of the extremities in a young woman with gigantism and obesity.

Various authors have pointed to the apparent association of acrocyanosis with ovarian[76][86][104][105] or thyreoid[41][65] dysfunction, but in view of what is now known regarding the control of both ovarian and thyreoid function by the pituitary, it would at all events be a simplifying assumption to attribute the alleged glandular dysfunction primarily to the pituitary. In our experience, however, the type of peripheral vascular disorder most commonly met with in myxœdema is the Raynaud phenomenon, not true acrocyanosis, and it seems probable that in susceptible persons the Raynaud phenomena would be readily excited in any condition in which the general matabolism was lowered. We are also unconvinced by the evidence of the association of acrocyanosis with ovarian disorder. As regards the pituitary, a more thorough study will have to be made of the vascular mechanism before the cyanosis which is sometimes observed can be classed as true acrocyanosis. We have met with patients whose condition on superficial examination resembled acrocyanosis, but who, on investigation, were found to exhibit the Raynaud phenomena.

Our case of acrocyanosis presents a number of features which at first suggest some disturbance of hypophyseal or hypophysiomesencephalic function. The combination of sexual dystrophy, emaciation, lowered matabolism and high sugar tolerance constitutes a picture in some respects resembling that of Simmonds's pituitary cachexia. On the other hand, the non-progressive character of the disease, the absence of anæmia and the good general health of the patient are against this diagnosis. Further, the sexual dystrophy, as already pointed out, is not of the typical glandular variety, for, although the disease has been present since early life, the bone age is normal, the patient has attained a normal (or rather diminutive) stature, and the bodily proportions are not eunuchoid. The presence of mental defect is also not readily accounted for by pituitary insufficiency. Glandular therapy in the form of "Antuitrin S" and thyreoid extract were without appreciable effect upon the cyanosis. While we do not consider that there is sufficient evidence in this particular case to support the hypothesis of the pituitary origin of the syndrome, the theoretical possibility has to be considered that some cases of acrocyanosis may be so caused. As Krogh[59] has shown, the tone of the capillaries depends upon an adequate concentration of pituitrin (vasopressin) in the blood. Deficiency of pituitrin in the peripheral blood would cause the relaxation of capillaries, but it would not account for arteriolar constriction. On the other hand, Cushing[22] has shown that when pituitrin is injected into the third ventricle it causes vaso-dilatation; an insufficient amount of pituitrin entering the ventricle might therefore have the reverse effect. The combination of arteriolar constriction due to insufficient pituitrin in the neighbourhood of the diencephalic nuclei on the one hand, with capillary dilatation due to insufficient pituitrin in the peripheral blood on the other, might therefore conceivably produce the vascular changes present in acrocyanosis. A deficiency of pituitrin secretion might have been expected to cause *diabetes insipidus* and this has not so far been reported in acrocyanosis. Also, ablation of the posterior lobe of the pituitary, either experimentally or as a result of disease, ought on this hypothesis to result in coldness and blueness of the extremities, but no correlation between lesions in this situation and vascular changes in the extremities has been established in man.

Cortico-Hypothalamic Mechanism. — As the hypothesis of endocrine dysfunction does not appear to explain satisfactorily all the features of our case, we are inclined to the view that the syndrome is of neurogenic origin, either cortical or hypothalamic. It is difficult to see how the type of mental defect present could be accounted for by a purely hypothalamic lesion, as the disturbance is intellectual rather than emotional. The mental changes would seem to point to some impairment of the function of the cerebral cortex. The reverse possibility, namely, that there is an impairment of the cortical control of hypothalamic function, would appear to have more anatomical than physiological evidence to support it, and may perhaps provide the simplest unifying hypothesis. There are various alternative nerve paths which may subserve the cortical control of the vegetative function of the hypothalamus.[15] Of especial importance for the present discussion are the connexions between the frontal pole and the hypothalamus. The corticifugal fibres from the frontal pole have intermediate cell stations in the medial nucleus of the thalamus,[15] the dorsal part of the *septum pellucidum*[80][109] and the *zona incerta* of the subthalamus,[15] whence they are distributed by second relays to various hypothalamic nuclei.[90][91]

A cortical defect in the frontal pole might cause not only mental impairment, but disturbances of

hypothalamic function, including changes in metabolism, sexual development and vasomotor control. If the defect was present in early life, as in the present case, it would be more likely to give rise to disturbances of growth than if the onset was at a later age. It is clear from this discussion, however, that more work will have to be done upon the relations between the cortex and the hypothalamus in respect of the control of vasomotor tone and other vegetative functions before this hypothesis can be regarded as satisfactory.

If the vasomotor disturbance, like the mental defect, were entirely of cortical origin, it would have to be explained by a concomitant defect of the neurones of the premotor cortex which subserve vasomotor tone.

Primary Ætiology.

Whatever be the seat of the disturbance in acrocyanosis, whether in the tissues, the vessels, the central nervous system or the endocrine glands, the question still remains as to what is the ultimate nature and ætiology of these changes. It would not appear justifiable at present to regard acrocyanosis as a specific disease, so that whatever conclusions we may come to with regard to the case under discussion will not necessarily apply to all cases. The early age at which the disease appeared, the absence of anything pointing to trauma or infection at any period of the patient's life, the family history and the presence of mental defect all point to the condition being developmental in origin—an agenesis or abiotrophy—and possibly inherited. Although several members of the family on the father's side had chilblains and blueness and coldness of the extremities, we cannot be certain that the vascular disorders from which they suffered were of a similar character to those of the patient, as we did not have an opportunity of examining any of them. The history is, however, sufficiently striking to suggest that some of the milder forms of acrocyanosis and forms appearing later in life may be incompletely developed examples of the same inherited anomaly. Such examples give very little clue to the fundamental character of the disorder; but when acrocyanosis shows itself as merely one feature in a syndrome which includes mental defect and disorders of growth and metabolism dating from infancy, the balance of evidence would seem to point to its being due to some error of development involving the cerebral mechanisms responsible for the control of vascular tone and other vegetative functions.

Diagnosis.

We do not propose to enter into the differential diagnosis of acrocyanosis in any detail, but there are certain points having a bearing upon the present discussion which call for comment, namely, the differentiation from Raynaud's phenomena and from cyanosis or erythema affecting the extremities in early life.

Acrocyanosis differs from Raynaud's phenomena in the following respects. It is symmetrical, diffuse and permanent (non-paroxysmal) and it may affect the face; there is an absence of blanching, trophic changes and pain; it affects a more distal segment of the vasculature, and the abnormal reactions of the vessels are abolished by nerve block.

When acrocyanosis occurs in early childhood it is liable to be mistaken for congenital heart disease. This diagnosis could be excluded in the case of our patient by the normal outline of the heart and vessels as determined by X ray examination and by percussion, the absence of cardiac murmurs and of clubbing of the fingers, the pressure of a normal oxygen saturation of the arterial blood and corresponding with this the bright red colour of the flare in response to injury or intracutaneous injection of histamine. The absence of clubbing is noteworthy, as clubbing has been ascribed to chronic oxygen lack as in congenital heart disease and anoxæmia from residence at high altitudes. Acrocyanosis differs from these two conditions, however, in that there is no arterial anoxæmia; the low oxygen tension develops only as the blood passes through the capillaries.

It is unlikely that acrocyanosis would be mistaken for pink disease in children, for, although the distribution of the discoloration may be somewhat similar, the colour in the two conditions in quite distinct; and in acrocyanosis there is an absence of the muscular hypotonus, the irritability and the photophobia, characteristic of pink disease. With regard to the similarity in the distribution of the lesions, it is of interest to note that there is a theory that pink disease is due to infection of the hypothalamic nuclei.

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Reports of Cases.

CARCINOID TUMOUR OF THE APPENDIX CAUSING ACUTE APPENDICITIS.

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Clinical History.

W.C., aged sixty years, was admitted on September 6, 1937, to the Newcastle Hospital with a history of having been seized with abdominal pain twenty-four hours previously. He stated that ten hours prior to admission he had vomited bile-stained fluid and that his pain was now of an aching type situated on the right-hand side of the lower part of the abdomen. His previous health had been fairly good, but on and off for the past five years he had at times felt a "strange feeling" in his abdomen accompanied by a spasm of aching pain. These attacks had soon passed off and he had felt none the worse afterwards. On examination he presented a picture of a well-nourished, elderly man with a temperature of 38·0° C. (100·4° F.) and a pulse rate of 96. Tenderness and slight muscular rigidity were present in the right iliac fossa, and his condition was diagnosed as acute appendicitis.

At operation the appendix was found to be partially retrocæcal and pointing towards the spleen. It was acutely inflamed, distended to the size of an adult thumb and bound down to the adjoining intestines. At the base of the appendix a hard nodule the size of a cherry could be felt. Because of the adhesions and the state of the appendiceal wall its removal was not easy, and as it was being delivered through the wound the appendix ruptured, filling the wound with thick yellow pus. The wound was closed and drained and the appendix, with the nodule at the base, was submitted to investigation. On opening up the lumen of the appendix widely it was seen that the dense rounded nodule was projecting from the lateral wall at the base of the appendix into the lumen, almost completely blocking it. The base of the appendix itself was healthy, but distal to the obstruction caused by the tumour the appendix wall was inflamed and necrotic in patches, while the lumen contained a good deal of thick pus. Macroscopically the specimen presented a typical picture of a diseased appendix obstructed by a tumour at the base and in a state of acute obstructive appendicitis.

The patient made a complete and uneventful recovery, his drainage tube having been removed after forty-eight hours, and he was discharged from hospital on September 28, 1937, with his wound soundly healed.

The pathological report and notes, for which I am indebted to Dr. T. F. Rose, are as follow:

> Longitudinally the section of the tumour shows a whorled arrangement of fibres similar to that seen in neurofibromata. The structure is that of a carcinoid of the appendix. The remainder of the appendix shows dense infiltration with inflammatory cells and extensive areas filled with red blood cells.

Comment.

This case is interesting in that it represents an example of carcinoid tumour of the appendix causing an acute appendicular obstruction in an elderly man, aged sixty.

Illingworth and Dick[1] state that carcinoid tumours of the appendix are considerably more common than adeno-

carcinomata, and are considered to constitute 0·4% of all appendiceal lesions found at operation. In Australia, from my own experience and that of other surgeons at the Newcastle Hospital, I would say that the percentage is even lower than this. Illingworth and Dick[1] give further interesting information on carcinoid tumours, of which the following is an abstract.

A carcinoid tumour may occur in any part of the appendix, and is especially common near the tip. Rarely two or three such tumours coexist. They occur commonly in young persons, especially between the ages of twenty and thirty years, and they are of particular interest in certain respects, for although locally invasive and possessed of certain of the microscopic features of carcinomata, they do not spread beyond the appendix and practically never metastasize. The tumour forms a hard, rounded, circumscribed nodule, usually small, and rarely exceeding the size of an almond, and it may be recognized on naked-eye examination by its characteristic golden yellow colour.

When small, the tumour lies in the substance of the appendix wall, and the mucous membrane over it is intact. When larger, it projects under the serous surface, and it may press upon and thus occlude the lumen. Occasionally a tumour at the base of the appendix has determined the onset of appendicular obstruction and acute appendicitis. In some cases, when the appendix is shrivelled and its lumen obliterated by fibrosis, the tumour assumes a central position.

Microscopically a carcinoid tumour is composed of solid masses of epithelial cells arranged in alveoli and supported by a stroma of connective tissue. Most of the cells are of spheroidal shape, with a central rounded nucleus and a fine reticulate protoplasm. In places the cells are columnar in shape, and arranged in palisade fashion. Yet again there are sometimes long, bulbous-headed, racket-shaped cells, which may be arranged in rosettes. Many of the cells contain cholesterol esters and other lipoids, and these are responsible for the golden yellow colour characteristic of the tumour. Other cells contain fine chromatin granules with a specific affinity for silver stains (argentaffin cells).

The tumour at first lies embedded in the muscle coat, and it spreads between the muscle bundles without destroying them. Often the tumour cells appear to be closely related to the nerve fibres of the myenteric plexus (Auerbach).

Origin of the tumour. Formerly the tumour was regarded as either a true carcinoma of low grade malignancy or a basal-celled carcinoma derived from the mucous membrane, but these views are now generally discarded, and at present the theories most widely held are those of Ehrlich and Masson. Ehrlich was impressed by the close relationship of the tumour cells to the nerve fibres of Auerbach's plexus, and on the basis of this observation and of the microscopical appearance of the cells he regarded the tumour as a neurocytoma originating in the autonomic nerves. Masson[2] has examined the microscopic character of the cells in great detail, and he has brought evidence to show that they are derived from the so-called Kulchitsky cells of the crypta of Lieberkuhn. These cells are believed to be of entodermal origin, but to be related intimately with the autonomic nervous system, and they are characterized by a specific affinity for certain silver stains. On the basis of his observations Masson has called the tumours argentaffin tumours, and has grouped them in the same cytological category with certain tumours of the adrenal medulla and of the paraganglia of the autonomic nervous system.

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Reviews.

PHYSIOLOGY AND BIOLOGICAL CHEMISTRY.

A TEXT-BOOK which has gone through thirty-five editions since 1848 hardly requires any introduction. Halliburton's "Handbook of Physiology" has had many editors. In 1896 the editorship was taken by Professor Halliburton. In 1928 Professor McDowall was secured to assist Professor Halliburton, and when Halliburton died McDowall became the sole editor. The aim of the editors from the beginning has been to produce a book suitable for medical students preparing for examination. To this end the treatment of the subject has been and still is rather didactic and dogmatic, although it has been somewhat less so under Professor McDowall's editorship. The new edition[1] gives a very good account of the present position of physiology and biological chemistry. Changes are apparent in almost every section of the book, and many new points have been introduced to keep abreast with modern developments.

A feature of the book, from the student's point of view, is the insertion in dark type of important points and figures which he should memorize.

It is a pity that references are not given to at least the most important papers on the various topics, for even an elementary student can gain much from looking up classical studies.

The author has attempted to give a compact conspectus of modern physiology and biological chemistry, and on the whole he has succeeded very well. Sometimes the treatment is so sketchy that wrong impressions might be gained; in other places details are given which might well be left for practical classes.

Few mistakes have been noted, and those not very important; for example, reduced hæmatin is not hæmochromogen.

It is interesting to see that Ehrlich's side-chain theory of immunity still survives.

The book can be recommended as an excellent text-book for junior students and could be read with advantage by many medical graduates.

DIAGNOSIS BY PHYSICAL EXAMINATION.

"PHYSICAL DIAGNOSIS", by Don C. Sutton, is a well-planned and attractively written book, in which direct examination of the patient is given pride of place in the diagnosis of disease conditions.[2] The object of the book is well expressed in the author's preface: "Notwithstanding the advances in the exact sciences the diagnosis of disease continues to be dependent almost entirely upon the history and the physical examination. This volume has been written to acquaint the student and the physician with the methods of examination by the use of the senses."

The first two chapters, an introduction and a history of physical diagnosis, are thoughtfully and earnestly written and eminently readable. "Hippocrates, twenty-three hundred years ago, his only armamentarium a keen perception of what may be seen and felt, described diseases so accurately that from his classification many of them may be recognized today. After twenty-one hundred years . . . Auenbrugger added the art of percussion to the methods of eliciting the physical signs of health and of

[1] "Handbook of Physiology and Biochemistry", by W. D. Halliburton, M.D., LL.D., F.R.C.P., F.R.S., and R. J. S. McDowall, M.D., D.Sc., F.R.C.P.; Thirty-Fifth Edition; 1937. London: John Murray. Medium 8vo, pp. 985, with numerous illustrations in the text, many of which are coloured, and four coloured plates. Price: 27s. 6d. net.

[2] "Physical Diagnosis: The Art and Technique of History Taking and Physical Examination of the Patient in Health and Disease", by D. C. Sutton, M.S., M.D.; 1937. St. Louis: The C. V. Mosby Company; Australia: W. Ramsay (Surgical) Proprietary Limited. Medium 8vo, pp. 495, with 293 text illustrations and eight colour plates. Price: 30s. net.

disease. Within the next fifty years Laennec invented the stethoscope, thus completing the basic methods of the observation of disease—history, inspection, palpation, percussion and auscultation. During the past fifty years we have added the assistance given by the modern sciences . . . Thus through the centuries . . . has been evolved the science and art of physical diagnosis."

The remaining seven chapters describe in detail the physical signs to be elicited from every part of the body by inspection, palpation, percussion and auscultation, their alterations in disease, and their significance in the building up by the synthetic method of "a disease picture which can be named and classified". Those portions of the book which are concerned with the lungs and heart contain a wealth of exact and carefully tabulated information as to appropriate physical signs. Those dealing with other parts of the body are from the very vastness of the subject rather sketchy, but in all cases the delightfully executed illustrations atone for the brevity of the text.

The book will be of most use to the senior student, but none the less of value as a reference book for the practitioner.

AN ATLAS OF BACTERIOLOGY.

DR. VAN ROOYEN has undertaken the task of editing the second edition of "Muir's Bacteriological Atlas".[1] The first edition appeared ten years ago and consisted of coloured plates drawn by Richard Muir to assist in the teaching of bacteriology at the University of Edinburgh.

One plate depicting *Piroplasma canis* has been omitted from the present edition, and an occasional plate differs slightly from that of the earlier edition. Twenty-six plates illustrating the morphology of thirty-two different micro-organisms have been added to the atlas, and Dr. van Rooyen is to be congratulated on maintaining the high standard set by the previous author.

The text has been entirely rewritten and considerably enhances the value of the book in that more adequate reference is made to the features illustrated in the plates.

The atlas clearly depicts the morphology of the majority of the common pathogenic microorganisms at magnifications usually varying from 1,000 to 1,500. Occasionally a magnification above or below these limits is used. With the variation in magnification the possibility of some confusion as to the relative size of microorganisms might result. For example, plates 11 and 12, illustrating *Brucella melitensis* and *Brucella abortus* appear on the same page, the magnification of the former organism being 1,500 and of the latter 900. The use of a more uniform magnification might even further improve a book that is already a valuable aid to the student of practical bacteriology.

NEW IDEAS ON CHRONIC DISEASES.

A NEW book on the "Treatment of Some Chronic and 'Incurable' Diseases", by A. T. Todd, physician to the Bristol Royal Infirmary, is at once well written, full of original and progressive thought in applied pathology, and very stimulating.[2] It is unfortunate that the author cannot conceal his contempt for "the primitive mentality still so current in medicine" and for "the majority of medical practitioners, who appear very loath to abandon the traditional therapeutics which have years of inadequacy to support them". The truth is that most practitioners are as anxious as the author to find better treatments; the author's contempt will not make them readier to accept his methods, which are not flexible or simple, and for which modifications of common drugs invented in Bristol are often necessary. The book contains chapters on sugar diabetes (the most interesting chapter in the book, in which the case for synthalin is presented), epilepsy, false phthisis (which contains dangerous doctrine for England, where early true phthisis is so often missed), asthma, Parkinson's syndrome (in which injections of colloidal sulphur are given with the object of improving hepatic function), toxic goitre, parenchymatous nephritis, "duodenitis" (according to the author 30% of the total of sick people investigated suffer from it, yet the condition is very little known), false heart disease (an admirable chapter), constipation, rheumatism, colitis and cancer. This is a book which must appeal to the scientific practitioner, even if he is not able or willing to carry out Dr. Todd's methods in every instance.

[1] "Muir's Bacteriological Atlas", enlarged and rewritten by C. E. van Rooyen, M.D.; Second Edition; 1937. Edinburgh: E. and S. Livingstone. Demy 8vo, pp. 106. Price: 15s. net.

[2] "Treatment of Some Chronic and 'Incurable' Diseases", by A. T. Todd, O.B.E., M.B., M.R.C.P.; 1937. Bristol: John Wright and Sons Limited; London: Simpkin Marshall Limited. Demy 8vo, pp. 211. Price: 10s. net.

Notes on Books, Current Journals and New Appliances.

A BOOK ON TREATMENT.

IN our issue of February 8, 1936, we drew attention to the second volume of "Modern Treatment in General Practice", issued by *The Medical Press and Circular*. The third volume has appeared, and is a worthy successor to those preceding it.[1] Its authors include many who are well known in British medicine, and the articles, which number fifty-one, cover an extremely wide range. For example, there are articles on the value of blood examinations in medical practice, on the treatment of injuries about the wrist joint, on the modern treatment of ringworm of the feet, on the treatment of essential hypertension, on the treatment of behaviour disorders in children, on the injection treatment of varicose veins, on the treatment of asthma, on the psychological problems in childhood, on the treatment of acute pyelitis, on dietetic essentials in general practice, and so on. This book cannot fail to be popular.

REGIONAL ANATOMY.

IN the issues of January 19, 1935, and June 12, 1937, we commended to readers the seven sections of an atlas of anatomy, published by Dr. E. B. Jamieson, Senior Demonstrator and Lecturer in the Department of Anatomy in the University of Edinburgh. The second edition of this atlas has now appeared and the first five sections are to hand.[2] The author is to be congratulated on the demand which his atlas has obviously created. In this edition the atlas is provided with a more suitable cover, and a table of contents is placed at the beginning of each section. More illustrations have been produced in colour, some of the illustrations have been enlarged, and several have been added. As stated in connexion with the first edition, the names used in the legends are those approved by the Anatomical Society of Birmingham in 1933, but in places the "B.N.A." terminology has been added in parentheses. This is an extremely useful atlas.

[1] "Modern Treatment in General Practice." Volume III, edited by C. P. G. Wakeley, D.Sc., F.R.C.S., F.R.S.E.; 1937. London: The Medical Press and Circular. Demy 8vo, pp. 448, with illustrations. Price: 10s. 6d. net.

[2] "Illustrations of Regional Anatomy", by E. B. Jamieson, M.D.; Section I: Central Nervous System (containing 48 plates); Section II: Head and Neck (containing 63 plates); Section III: Abdomen (containing 37 plates); Section IV: Pelvis (containing 33 plates); Section V: Thorax (containing 30 plates); 1937. Edinburgh: E. and S. Livingstone. Double foolscap 8vo.

The Medical Journal of Australia

SATURDAY, DECEMBER 18, 1937.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

PSYCHOLOGY AND THE GENERAL PRACTITIONER.

THERE has recently come to our hands a pamphlet issued by the Medical Society of Individual Psychology, of London;[1] in this booklet various writers discuss the value of psychological methods to the ordinary practitioner in his everyday work. It cannot be doubted that medical men are now showing a growing interest in the subject and are making a psychological approach to certain problems; this is the general impression left upon the reader's mind. But there still remains more than a sprinkling of doctors who, if not actually hostile, are at least far from interested in the great increase in psychological knowledge which has taken place since the beginning of the present century.

One of the chief reasons for this neglect is that the science, when first it was seriously considered as a science, was essentially Freudian; and Freud, thirty years and more ago, was derided by many, though his disciples are now numbered by the thousand, and not only medicine, but literature and art have been affected by his work. Nevertheless, the fact that he was an innovator in a difficult field and a pioneer in a subject involving a difficult technique and the use of a new phraseology induced a state of mind unfavourable to the spread of psychology amongst general practitioners. Of Freud's articles of faith it may be briefly said that, in his view, desires once active live on, and that particular situations, once experienced, persist in the individual to emerge at intervals as the content of dreams or in other ways. The beliefs of Freud, particularly in their implications in matters of sex, have more than once led to revolt among the ranks of his pupils, notably in the cases of Jung and Adler. Freud insists that both Jung, with his "analytic psychology", and Adler, the originator of "individual psychology", have wrongly rejected the prime importance of sex desires in the neuroses and, indeed, in life generally. To Adler, the fundamental fact in the genesis of the neuroses is a feeling of inferiority. He considers the self-assertive impulse, and not that of sex, to be the great positive force in life, and that which is most likely to be frustrated by the individual's own sensitiveness or by his environment; it is at once the source of achievement on the one hand and of maladjustment or misconduct upon the other.

Whatever the truth, it is certain that Adler's theories form the basis of much useful neurological treatment, and his method of individual psychology is that approved and employed by the society to whose booklet we have referred. A point which may be stressed is that there seems to be no cogent reason why the general run of medical men should not inform themselves upon the essentials of these methods of treatment, if only to the discomfiture of a not inconsiderable band of quacks.

Our knowledge of physical ills and their treatment has made satisfactory progress during our own day and will further increase; but we live in an age which becomes increasingly mechanized and which many believe to be overhung by the hideous perils

[1] "The Parent-Child Relation: The Psychological Background and Other Papers", by H. G. Baynes, S. Crown, S. H. Lubner, A. C. Court, M. Marcus and F. G. Crookshank; 1937. London: The C. W. Daniel Company Limited. Medium 8vo, pp. 71. Price: 2s. 6d. net.

of modern war, a state of affairs which must bring mental evils in its train. Surely, then, the medicine of the future will be increasingly bound up with the investigation of psychological problems presented by patients of all classes, and this whether these problems go hand in hand with organic disease or not. It is likely that a generation or two of students will need training of this sort before their work will have its effect; but it is a healthy sign that at one large Australian hospital an admirably equipped block for the housing of patients likely to benefit from psychotherapy is to be built in the not-too-distant future.

There is small doubt that the general practitioner, if he can but grasp the opportunity for training in the subject, can carry out a great deal of useful psychological work. He it is who sees common psychical disorders at the start. His efforts may commence amongst babies and infants; he can treat the day-dreams, the vague anxieties and the self-consciousness of the adolescent; he can help to resolve the difficulties so common between father and son or husband and wife; he has the chance of learning of all those factors which make family life unhappy or the reverse. We are told, till the statement wearies us, that the suburban doctor's work is gradually vanishing before his eyes; the fact remains that in the realm of preventive psychology he may one day reign supreme. The science of psychology grows in value every day, and its greatest value in the future will be in the field of prevention.

Such a welcome addition to the current fund of general knowledge in these matters will ensure that patients who are afflicted with the more severe psychoses or with symptoms of psychological origin which seem to be profound and fixed, will be saved much unnecessary suffering by early reference to a specialist in psychopathology. In England and other countries there is now a widespread and growing demand for psychotherapeutic instruction on the part of general practitioners; the day has gone when psychiatry meant only the study of hopeless psychoses seen at a late stage. Modern psychology has mapped and surveyed large areas previously unknown, and the science of the study of behaviour is now founded upon a solid stock of knowledge. The cultivation of these new interests will need expert guidance and control in their clinical applications, but they are bound to bring the practice of medicine into closer relationship with life and its greatest problems.

Current Comment.

EPIDEMIOLOGY OF STREPTOCOCCAL INFECTIONS.

W. H. BRADLEY, a research worker from the Department of Medicine at Cambridge, has recently published a valuable paper on certain aspects of the streptococcal infections as studied by him in New York.[1] The work, the author states, is not intended to be a survey of the whole field of streptococcal epidemiology, but represents the results of an exploration conducted in a restricted field—that of the family—as well as a consideration of the carrier problem and an analysis of the types of hæmolytic streptococci met with in these population groups.

Bradley considers that hæmolytic streptococci may be found in the throats of 20% of the population, and that most of these organisms are highly pathogenic to man. They fall into a number of distinct serological types, but the prevalent types are variable from time to time and place to place. Clinically, a streptococcal naso-pharyngitis or a follicular tonsillitis may be present in a given patient without any of the classic signs and symptoms; and the same may be said of apyrexial colds.

In Bradley's opinion, streptococcal infections of the upper respiratory tract spread very slowly. Sharp rises in the incidence of these diseases in epidemic form are rarely met with, but their occurrence should direct attention to the milk supply. In the family form of epidemic it was constantly noted that any individual outbreak was invariably due to a single type of streptococcus. This organism, of which rather more than thirty types are now known to exist, is believed to be one of the most widely spread and lethal agents in human disease; but we are as yet ignorant of many facts concerning its epidemiology. As has been pointed out in these columns, present methods of treatment involve the outlay of large sums of money for the isolation, in special buildings, of persons presenting manifestations of the streptococcal disease called scarlet fever; but we neglect to consider the epidemicity of a disease which produces apparently isolated cases of puerperal fever, septicæmia or mastoiditis—all dangerous expressions of the one

[1] *Guy's Hospital Reports*, July, 1937.

basic phenomenon, the presence of streptococcal infection in endemic form. We should be wise to consider every case of streptococcal tonsillitis as the token of a serious disease possessing an epidemiological gravity at least equal to that of diphtheria.

Although more than thirty types of the *Streptococcus pyogenes* have now been identified, it appears likely that at any one time in a given community any streptococcal outbreak is caused by one type of the organism alone. The instance is cited of a school of three hundred boys, in which, during five years, there were six epidemics of streptococcal disease, each clinically distinct from the others. A logical corollary is that there is no element of pure chance in the occurrence of cases, allegedly sporadic, of acute rheumatism, mastoiditis or puerperal fever; and the investigations of Colebrook strongly support the view that infections of the upper respiratory tract are an important factor in the pathogenesis of these diseases.

Since these cocci occur in such a multiplicity of types, each type possessing specific antigenic properties, it follows that the preparation of effective therapeutic sera is a complicated task, since we have to deal, not with one, but with thirty or more infections. These are probably dust-borne in part, and probably also spread occurs through the medium of "droplets", a plain indication that the isolation of established cases of the disease will be much less effective than the protection by adequate spacing of all contacts. Only thus can the danger due to "carriers", all suffering from subclinical infections, be provided for. There is also an urgent necessity that all rheumatic subjects should be carefully protected against naso-pharyngeal infections.

CYANOSIS AFTER ADMINISTRATION OF SULPHANILAMIDE: ITS CAUSE AND TREATMENT.

AT the present moment, "Prontosil" and its competitors and their derivative sulphanilamide are being zealously prescribed for almost any infective process, streptococcal or otherwise. While it is necessary to extend the applicability of this subject to its utmost, it is equally important to realize that such extensive use of the drug must produce a number of instances of poisoning, as a result of overdosage or idiosyncrasy. Many reports have already appeared in which cyanosis, dyspnœa, agranulocytosis *et cetera*, have become manifest after the exhibition of sulphanilamide or a sulphanilamide-producing agent. The cyanosis may be due to the development of either methæmoglobinæmia or of sulphæmoglobinæmia, which are distinguishable spectroscopically. The method of production of methæmoglobinæmia is not clear, but fortunately it has not proved to be a formidable complication. The production of sulphæmoglobinæmia has recently been the subject of investigation by H. E. Archer and G. Discombe of Saint Bartholomew's Hospital, London.[1] It appears that sulphanilamide is one of a series of catalysts which facilitate the change from hæmoglobin to sulphæmoglobin as the result of bacterial putrefaction in the colon and the consequent production of hydrogen sulphide. The time that will elapse before sulphæmoglobin is detected will depend, of course, upon the amount of hydrogen sulphide absorbed from the gut, on the nature and quantity of the catalyst administered, and on the delicacy of the technique available for the detection of hæmoglobin. The reaction was produced without difficulty *in vitro*; but it was necessary to use much greater concentration of catalyst than possible *in vivo*, and to use only traces of sulphide to keep the reaction from too rapid completion. Discombe produced sulphæmoglobinæmia in himself by taking sufficient sulphanilamide and calx sulphurata together.

The reaction is accelerated by the taking of magnesium sulphate. Archer and Discombe discount the possibility of a direct conversion of the sulphate to sulphide in the bowel, but consider that the additional water attracted to the colon and the rapid passage of partially digested food to the colon favour the production of large amounts of hydrogen sulphide by bacterial action. Any treatment which helps the formation of a liquid stool may therefore be expected to accelerate formation of sulphæmoglobinæmia. The authors suggest a *régimé* for patients receiving sulphanilamide which consists of the provision of a low residue diet of adequate caloric value, and the administration of 30 to 45 cubic centimetres of liquid paraffin per day. All other aperients are forbidden, but enemata are used if necessary. One further precaution is desirable, and that is the omission of any phenacetin, which may cause further cyanosis by the development of methæmoglobin. Archer and Discombe emphasize the great importance of a spectroscopic examination of the blood serum if a patient receiving sulphanilamide develops cyanosis. The spectroscopic test is seven times more sensitive than clinical examination. It also serves to distinguish the cause of the cyanosis, and will hence be an important guide to further medication. If necessary, simple methods exist for the approximate quantitative estimation of sulphæmoglobin.

The practical value of this paper is considerable. Magnesium sulphate and drugs of the coal tar series are prescribed very commonly in febrile conditions. The practitioner must be watchful to exclude them before giving sulphanilamide, particularly as it is impossible to forecast how long patients may have to continue taking the dye. The loss of the oxygen-carrying property of the blood following upon sulphæmoglobinæmia may conceivably be sufficient to turn the tide of a streptococcal septicæmia against the patient's recovery. It is equally important to be aware of the presence of methæmoglobin in the blood, thereby to be encouraged to persist in the use of what sometimes seems to be life-saving medication.

[1] *The Lancet*, August 21, 1937.

Abstracts from Current Medical Literature.

THERAPEUTICS.

The Parenteral Administration of Liver Extract in Pneumonia.

ADMITTING that a series of thirty cases is too small for general deduction, J. Alfred Wilson and William C. Carey (*The American Journal of the Medical Sciences*, June, 1937) record their experiences in the use of liver extract for the stimulation of leucopoiesis in pneumonia. It has been demonstrated that the parenteral administration of liver extract increases the leucocyte count in normal individuals (as much as 94% in ambulatory persons); the peak of the rise was reached in about seven hours and slowly returned to normal. The mortality rate in this series was 17%; this is regarded as favourable, as the prognosis was not good in all cases. The mortality rate in all cases of pneumonia for one year in the hospital where the authors worked was 33%. The average increase in the total leucocyte count was 70%, all but six patients responding. The improvement in the blood count was paralleled by clinical improvement and greater urinary output. The average amount of liver extract administered intramuscularly was 6 cubic centimetres a day; injections were given at intervals of six to eight hours. Oxygen, expectorants, sedatives and stimulants were given as the various indications arose. The authors state that the treatment is safe and simple to give and causes no anaphylactic reaction. The pain at the site of injection is of short duration.

Purine Derivatives in Angina Pectoris.

M. G. BROWN AND J. E. F. RISEMAN (*The Journal of the American Medical Association*, July 24, 1937) discuss the value of purine derivatives in the treatment of *angina pectoris*. Theophylline and theobromine have been widely used in recent years in combination with other preparations for *angina pectoris*. The results of such treatment have not been carefully assessed. Seventeen patients were treated with various preparations of this kind: theophylline by itself, with calcium salicylate, with ethylene diamine and others. The beneficial effects of these preparations were apparently mainly due to the theophylline. Theophylline and theobromine were most effective when given frequently and in rather large doses. Unfortunately in such cases nausea and heartburn occurred, and the improvement disappeared. The best results were obtained when the largest doses were given short of causing nausea. Theobromine with sodium acetate, in doses of 0·5 gramme (seven and a half grains), four times a day, was far superior to all other preparations of theobromine and was as effective as the best of the theophylline compounds. Theobromine with calcium salicylate in a dose of 1·0 gramme (fifteen grains) was of value; but theobromine in a dose of 0·3 gramme (five grains) and theobromine with 0·5 gramme (seven and a half grains) of sodium salicylate were less effective than other preparations. Caffeine citrate was of little value in *angina pectoris*. Theobromine with phenobarbital, and theophylline mono-ethanolamine, marketed as "Theominal", and theamin with "Amytal" gave no better results than separate treatment with theobromine and phenobarbital; the combination of these two drugs in one capsule was not recommended. Patients with angina were tested to ascertain whether their exercise tolerance increased under treatment. Theophylline and theobromine sodium acetate were most valuable; the latter was by far the least expensive. Sedatives were helpful at times in *angina pectoris*; but their combination with a purine derivative did not result in an increased exercise tolerance, and rendered it difficult to vary the dose of the two preparations independently.

The Therapeutic Properties of Cobra Venom.

R. N. CHOPRA AND J. S. CHOWHAN (*The Indian Medical Gazette*, June, 1937) discuss the therapeutic properties of the venom of the Indian cobra (*Naja tripudians*). Cobra venom possesses a proteolytic ferment; when injected intravenously it damages the *tunica intima* of the blood vessels, causing hæmorrhage. In 1931 White showed that cobra venom had a destructive action on granulation tissue; he made aseptic spaces in the muscles of rats and introduced various irritant substances, including cobra venom; at the end of a week he observed that granulation tissue had formed in all the spaces excepting those containing cobra venom; these spaces had in fact increased in size. In 1934 Rousseau showed that the tissue-destroying property was due to a lysocythin ferment, derived from a phospho-diastase when the venom was heated to 70° C. In 1936 Chopra, Das and Mukherjee showed that cobra venom in a dilution of 1 in 60,000 or 1 in 80,000 stimulated the growth of tissue cells in culture, but in a dilution of 1 in 20,000 caused the destruction of growing cells. From this the conclusion may be drawn that the injection of cobra venom should be of value in the treatment of neoplasms; but it would have to be injected directly into the neoplasm, otherwise it would not be in sufficient concentration to destroy the neoplastic tissue. In 1931 Chopra and Ishwariah, experimenting with cats, reported that cobra venom produced an initial rise of blood pressure, followed by a fall. In 1935 Link reported that the venom of the Indian cobra had no blood-coagulating principles; in fact it destroyed the thrombokinase. In 1932 Kellaway and Holden showed that cobra venom had a curara-like effect on motor end-plates. The use of cobra venom has been advocated in the treatment of trigeminal neuralgia and various other neurological conditions. The authors have shown that the instillation of a 1% solution of cobra venom into the conjunctival sac of a rabbit produces irritation, followed by acute congestion, lachrymation and œdema. The subcutaneous injection of 0·01 to 0·015 milligramme in man causes contraction and rigidity of the pupil; in some cases there is a slight diminution of the intraocular tension, and the arterioles of the *fundus oculi* appear to be slightly dilated (Baillart and Koressios, 1934). Koerbler administered cobra venom to 26 patients suffering from neoplasms; all the injections were painless and none caused a reaction; there was great relief from pain. In the treatment of a malignant growth of the face the combination of radium and cobra venom caused more rapid absorption and relief from pain than the use of radium alone. The experiences of a number of other authors in the treatment of malignant disease are quoted. A preparation of arsenic and dead cobra has been used in northern India in the treatment of patients suffering from leucoderma and syphilitic eruptions. Cobra venom has been used in Hindu medicine in leprosy. Labernadie and Branbilla have mentioned its use also in neuro-syphilis, metasyphilitic eruptions and neuroleprosy. The authors consider that it is doubtful whether the venom has any direct action on lepra bacilli or spironemata. They go on to describe the method of preparation of the venom for therapeutic use, and set out the dosage. There is sometimes a local reaction after injection, consisting of inflammation, itching and swelling; when large doses are used hæmatomata may form. In rare instances there may be a generalized reaction, consisting of malaise, slight pyrexia, giddiness, nausea and, perhaps, diarrhœa. The authors have treated over 100 patients by injection of cobra venom during the past two years. They report a number of cases. The injections were given intramuscularly, twice a week, one half to one mouse unit being given at first; the dose was gradually increased to ten or even twenty mouse units. Relief from pain as a rule was appreciated after the third or fourth injection; in addition the patients experienced improvement in health and increase in appetite. In some cases the injection of saline solution was substituted; but in each no relief from pain was experienced while these injections were continued. Patients with vague pains, neuralgia, lumbago and myalgia often improved considerably. Patients with nervous leprosy obtained great relief from pain and paræsthesiæ. Patients with

newgrowth obtained relief from pain, but were not cured. The electrical responses in some cases of paralysis improved; but this may be attributed to massage and electrical treatment. There were no untoward effects, and there seemed to be no tendency to addiction.

NEUROLOGY AND PSYCHIATRY.

Anxiety Attacks in Children.

WILLIAM S. LANGFORD (*American Journal of Orthopsychiatry*, April, 1937) studies the anxiety attacks in twenty children, sixteen of whom were girls, and whose ages were all below fourteen years. The duration of the illness varied from two weeks to four and a half years. The majority of the children were between eleven and fourteen years old at the onset of the attack and showed evidence of early development of the secondary sexual characteristics. The symptoms exhibited by the children are similar to those seen in adult anxiety cases, the attacks consisting of varying combinations of these symptoms with symptoms referable to some particular organ occupying the foreground. Two cases are reported in detail. Therapeutic efforts were followed by improvement in eighteen out of the twenty cases. The author stresses the necessity of a thorough physical examination in order to eliminate organic disease, which anxiety symptoms frequently mimic. Treatment of the child is of more value than the treatment of symptoms. The author believes that anxiety attacks are not uncommon in children, particularly in seriously minded pubescent girls, who may have previously shown personality disorders: timidity, shyness, enuresis and an over-concern about health. The anxiety attack is frequently precipitated by death of a relative, tonsillectomy or other exogenous factor. Chronic invalidism is apt to develop if such a child, with an anxiety state, is treated for an organic illness which is not actually present. Due weight must be given to the emotional factors in nearly every pædiatric problem.

Spontaneous Intraspinal Subarachnoid Hæmorrhage.

HOWARD B. SLAVIN (*The Journal of Nervous and Mental Disease*, October, 1937) reports in detail a case of spontaneous intraspinal subarachnoid hæmorrhage. Intracranial subarachnoid hæmorrhage from causes other than trauma is well known; but the occurrence of such hæmorrhage within the spinal canal is very rare. Only two other cases seem to have been reported. The author's patient was a male, aged forty-five years, who was suddenly smitten with pain in the region of the left hip when walking across the room. Except for the presence of Kernig's sign, physical examination revealed no abnormality. The previous history did not suggest a hæmorrhagic diathesis. Biochemical tests also revealed no abnormality. Blood-stained fluid was obtained by lumbar puncture. There was evidence of a subarachnoid block. The cerebrospinal fluid was sterile. The patient was discharged, free of symptoms, five weeks after admission to hospital.

Gargoylism.

W. R. ASHBY, R. M. STEWART AND J. H. WATKIN (*Brain*, June, 1937) report two cases of chondro-osteodystrophy of the Hurler type. This syndrome consists of mental deficiency, dwarfism, deformity of the limbs, corneal opacities, and enlargement of the liver and spleen. The condition was first observed in 1919 by Gertrud Hurler. Other cases of this rare dystrophy have been reported in the literature. On account of the large head and grotesquely inhuman features the condition has been called gargoylism. In both cases in the present report pronounced enlargement of the pituitary gland was found; both thyreoids were abnormal. The ganglion cells throughout the entire nervous system showed great alteration; the Nissl granules were reduced in number and the cell nucleus was dislocated to one side. Chemical analysis of the brain in one case showed a marked reduction of cerebrosides. A comparison of the histological changes in gargoylism with those of amaurotic idiocy is given, and other comparisons are made between this condition and such other congenital conditions as Gaucher's disease, Niemann-Pick's disease and Schüller-Christian's disease. The majority of patients with gargoylism so far described have been low-grade imbeciles. Family histories were not exceptional, and the parents were almost invariably healthy.

The "Cardiazol" Treatment of Schizophrenia.

P. SCHEUHAMMER AND L. WISSGOTT (*Psychiatrisch-Neurologische Wochenschrift*, June 26, 1937) report the results obtained in a series of thirty cases of schizophrenia in which treatment with "Cardiazol" according to the method of Meduna was used. The series comprised nineteen katatonic, three hebephrenic and eight hallucinated paranoid patients. The hebephrenic group showed the poorest response to the treatment; no essential difference in response was apparent between the two other groups. The duration of the illness appeared to be of greater prognostic importance than its clinical form. Thirteen (43%) of the thirty patients treated had a complete or almost complete remission. A complete remission was obtained in nine (69%) of the thirteen cases of less than one and a half years' duration, but in only four of the seventeen older cases. In these four the illness had run a strongly remittent course, and the duration of the current attack was less than one and a half years. In the majority of cases the remission set in after a few seizures and required only one to two weeks for its full development. If no result was obtained after fifteen to twenty seizures treatment was abandoned. There were three relapses in the series. The authors conclude that the "Cardiazol" therapy of schizophrenia is well worth a trial on a more extensive scale.

Personality and Chronic Arthritis.

GOTTHARD COHEN BOOTH (*The Journal of Nervous and Mental Disease*, June, 1937) sets out to describe the psychological character of patients suffering from chronic arthritis. The examination of case histories shows a similarity in the reactions of these patients to certain situations in life and, in the author's opinion, points to a fundamental similarity in their personality. To demonstrate this he performed the Rorschact test upon twenty-two of his patients. He concludes that the dynamic predisposition to acquire chronic arthritis rests upon: (i) an urge to be active, manifested chiefly in the extrapyramidal system; (ii) low general vitality; (iii) inadequate response of the vasomotor system, the response to temperature changes being physically inadequate and to emotional encounters psychologically inadequate; (iv) an urge to remain independent of environmental influences, due to circumstances in childhood that caused the development of a neurotic defensive attitude. The author believes that the pathological changes of chronic arthritis constitute a regressive method of pursuing the original life plan. Once the individual has proved too weak to maintain his security from external interference by activity, the muscles are relieved of their burden by the passive stiffening of the joints. A therapeutic approach is possible, based upon an appraisal of the dynamic relationship between the individual and his environment.

Prefrontal Leucotor in Mental Disorders.

EGAS MONIZ (*American Journal of Psychiatry*, May, 1937) outlines a surgical procedure that, he believes, is beneficial to patients suffering from mental disorders. The operation is designed to interrupt the connecting fibres between cells of the prefrontal area and other regions, that is to say, by sectioning the subcortical white matter. The author admits that the hypothesis underlying his procedure may be questionable, even audacious; but he believes that his results justify his daring. He uses a special leucotome, and through trephine openings cuts a number of cores from the subcortical white matter. Full surgical details are presented and three cases are reported. Post-operative neurological disturbances are merely transitory. Mentally deteriorated patients obtain no benefit. Schizophrenic and paraphrenic patients have recovered and have been enabled to return to former occupations.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on September 1, 1937, at the Medical Society Hall, East Melbourne, PROFESSOR R. MARSHALL ALLAN, the President, in the chair.

Traumatic Emergency Surgery.

The meeting took the form of a symposium on traumatic emergency surgery.

DR. A. E. COATES read the opening contribution, in which he dealt with the traumatic emergency surgery of the limbs.

Dr. Coates said that the object of the symposium was to meet a desire on the part of some practitioners for help in the handling of injuries in workmen. The new *Workers' Compensation Act* provided for medical attention to injured workmen within certain limits, and it was hoped that in these cases, which had been usually the burden of the public hospitals, the patients would come under the care of their own doctors. There was a certain amount of traumatic surgery which could be reasonably undertaken by the attending practitioner, and it was desirable that the latter should be informed of the modern methods employed and that he should equip himself in every sense of the word if he was to deal with these cases.

Dr. Coates said that in the short time at his disposal he proposed to deal with a few typical injuries of the hands, emphasizing certain general principles in treatment. The adherence to these fundamental principles was of great importance in restoring a workman in minimal time.

In all injuries of the hands or forearm in which the skin was torn or cut (and these were increasingly common in modern industry) it was essential to arrest hæmorrhage and to apply some antiseptic dressing to the damaged tissue. This was generally done as a first aid measure in factories. It was well to realize that a workman's hand was almost as important as his brain. It was the tool he employed, and every effort should be made to preserve the instrument upon which his livelihood depended.

There was a tendency to regard minor hand injuries as of little importance, but the sequelæ were often so serious and the disability from neglected simple lesions was so crippling that the greatest care should be exercised in the treatment of these conditions. If there was any difficulty in adequately cleaning up a hand the practitioner should not hesitate to give a general anæsthetic. The hand was extremely sensitive, and thorough examination and repair were often impossible without narcosis. Simple incised wounds might be sutured loosely after being cleared up with ether soap, spirit, benzine and some antiseptic such as "A.C.M." or flavine. Soap and water were better than any antiseptic. On the fingers it was not advisable to cut away edges of skin, as there was little enough to act as a normal cover. If the edges were bruised strapping should be applied without sutures. Pulp and lateral cuts did not heal well, as every surgeon knew who had attempted to suture a tendon in the finger. Œdema and post-operative swelling caused tension of sutures and gaping occurred. Clean cuts, however, might be sutured with horsehair, but not tightly. When a piece of skin had been cut off as a bread slicing accident, an immediate graft of a bit of skin could be done. Firm strapping should be applied with a little plaster of Unna's paste, and the wound should be left alone for two or three weeks. Care should be taken in suturing not to pick up digital nerves. After-pain (causalgia) might occur and prove very intractable.

Lacerated wounds were very common. The crushed finger was a problem. If the end phalanx was comminuted and the soft tissues were crushed beyond repair, amputation proximal to the fracture might be indicated. Perhaps enough skin of the pulp was left to cover the stump. Preservation of the proximal end of the third phalanx would give a stronger finger, owing to the attachment of the long flexor tendon. If the finger had been amputated cleanly (accidentally) the stump should be dressed and no further amputation should be undertaken. Bone should not be taken away merely to produce the orthodox skin flaps. Guillotine amputation and strapping applied later (no sutures) would produce a good cover for the stump, and a small graft would give a good result in doubtful cases. Tendons should not be sutured over the ends of cut bone. With regard to amputation of fingers, Dr. Coates quoted the words of Willems: "Even the smallest portion of a distal phalanx lost from the tip of any finger constitutes a lamentable loss from trained hands."

Dr. Coates went on to say that it was sometimes argued that the proximal half of the end phalanx was not much good to the patient, and that if it was left the patient was deprived of the compensation he would obtain if the whole phalanx was removed. The implications of that argument would not bear serious examination. The attempt to suture the stump of an amputated finger when the skin was too scanty was seen in illustrations shown by Dr. Coates: necrosis of tissue, sepsis, osteomyelitis, sequestrum formation and further loss of tissue and delayed healing resulted.

In laceration of skin of the dorsum of the hand—often the skin was bruised and pulped—no attempt should be made to undercut the skin and draw the edges together tightly. It was most essential to leave the tissues as free from tension as possible. Œdema was certain to occur and increase of tension resulted. Dead skin should be cut away and the wound left open. Mild antiseptic dressings over waxed gauze ("Parawax") should be applied with a splint.

Dr. Coates then discussed lacerations of the palm. In bursting of the palmar skin with tearing up of a flap hæmorrhage was not often a feature. The wound should be cleaned and no suture need be applied; sutures were worse than useless. Gauze soaked in flavine should be used and a splint should be applied. Healing would occur perfectly without the sepsis which generally accompanied suture of the palmar skin after accidents. If an area of the palm had been denuded, grafting of the hip pocket type could be done later.

Discussing fractured phalanges, Dr. Coates said that the nature of the accident should indicate a fracture. In all doubtful cases of hand injury an X ray examination should be made. The principles applying to these fractures were the same as elsewhere in the body; the four "R's"—recognition, reduction, retention and reeducation—were the requisites. Fractures of the end phalanx caused no trouble—they were often comminuted. The second and first phalanges caused trouble if the fracture was of the transverse type. Anterior bowing was often seen, and if it continued it interfered with the function of the flexor tendon in its osteo-fibrous canal. The fracture should be reduced and the splint applied with the digit in flexion. The straight finger splint was a relic of the past and could not be too strongly condemned. The finger should always be put up in a position of function, in other words, in flexion. Traction of the finger by strapping or by penetrating wire with the hand flexed might be necessary (Böhler method). Failure to reduce a fracture in the early stages was often a cause of non-success in these cases. A small plaster splint applied with the finger flexed would often keep these fractures reduced. Bad results often necessitated amputation of the finger. The second finger should not be amputated if it could be possibly avoided. It was a key structure in the hand and was more important than the index finger. The thumb or any part of it should never be amputated; it should be allowed to slough off if it would, but no part of it should be removed. If the little finger, or for that matter any finger, was to be amputated, no operation should be performed in the presence of sepsis, for fear of infecting the ulnar bursa (tendon sheath) with subsequent loss of function of the hand. If an amputation was being performed through the nail bed, care should be taken to remove all the remnants of nail tissue; an irregular growth of nail was often a

source of delay in the restoration of the patient. It might be necessary to excise all the nail bed and nip off the tip of the end phalanx in order to cover the nail bed with a cap of skin (as was done for ingrowing toe nail). Care should be taken not to destroy the dorsal tendon insertion.

Dislocations of the end phalanx were often not recognized. A lateral X ray picture was necessary. Reduction was easy in the early stages; a splint should be applied with the finger in flexion, and results were good; but if these dislocations were neglected they were a source of disability. Dislocation of the first phalanx of the thumb on the metacarpal head generally occurred backwards. The dislocation should be reduced and the thumb put up in extension. If the dislocation recurred, a rent in the capsule might require suture.

Dr. Coates then discussed foreign bodies in the hand and fingers. He said that brass filings, glass *et cetera* were often embedded in the hand. In any case of cut by glass or loose metal an X ray examination should be made; glass would be seen. Wounds should be left to heal by second intention. A nodule might later form, enclosing the foreign body, and incision might be made to remove it. This operation might be very difficult. If a needle was the foreign body, a transverse cut should be made across it and it would be found. The tendon sheath should be avoided; the surgeon should work under a tourniquet, and if possible visualize the needle under the X ray screen and insert two needles at right angles down to it. The wound should be left open after removal of the foreign body. Organisms might be stirred up, and if the wound was closed infection was locked up. If infection beneath the skin occurred, a longitudinal incision should be made—parallel with the important structures, vessels, nerves and tendons—and there was little chance of injuring them.

Dr. Coates said that he did not propose to deal with the problem of hand infections, but would impress on those present the importance of recognizing the fact that severe infections, which might endanger life or limb, might result from trivial injuries. No punctured wound of the hand by needle, metal filing, fish scale or splinter was too small to be neglected. Thorough cleaning up of the wound, splinting the finger or hand in the position of function, and the application of hot foments if pain continued, would often cause an incipient lymphangitis to resolve. If the hand became red and swollen and the dorsum œdematous within twenty-four hours of such an injury, the hand should not be indiscriminately incised. It should be rested on a plaster splint, foments should be applied, and the patient should be put to bed. Pus did not form overnight. Baths were not good; maceration of the skin occurred. Foments and splinting were the rational treatment. If suppuration occurred in a tendon sheath or a fascial space, a very serious complication had developed and the treatment required expert management. Dr. Coates did not propose to discuss this complication.

Bruising of the palm of the hand might cause a collar-stud abscess to develop, again pregnant with possibilities of mischief. The skin over the palm, over the heads of the metacarpal bones was the common site, being hard and horny; a tender area developed some days after a slight injury. It should be remembered that the abscess beneath the cuticle often communicated by a narrow track with a collection of pus in the fatty tissue, and this abscess had to be opened. Spread via the web to the dorsum might occur. Incision of the web between the fingers could not do much harm. General anæsthesia was necessary for all surgery on infected hands.

Dr. Coates said that he would omit any reference to divided tendons or nerves, as he regarded these injuries as serious and requiring specialist attention. If a divided tendon was discovered in the course of what appeared a trivial wound, the method of suture was indicated by illustrations which he showed. Prolonged splinting in a position allowing relaxation of the affected tendon for at least four weeks was necessary. Dr. Coates had seen the proximal end of a cut median nerve sutured to the distal end of a flexor tendon. Rupture of the tendinous attachment of the extensor of the finger to the third phalanx might be effectively treated by putting the finger up with the first interphalangeal joint flexed to a right angle and the end joint hyperextended. The finger should be left in a small plaster cot for four weeks.

Injections of antitetanic serum (1,500 units) should not be omitted in all cases of cut or lacerated dirty hands, especially when the wound was of the punctured type.

Dr. Coates had never seen a successful repair of a cut flexor tendon in the finger with a perfect end result. He had seen a few in the hand, but most at the wrist. Divided flexor tendons gave good results if sutured early at the wrist, fairly good results in the hand and bad results in the fingers.

Tendon sheath infection of the fingers by the *Staphylococcus aureus* generally ended in loss of the tendon and a stiff finger. This finger might be a nuisance to a workman and its amputation might be necessary. It was wise to wait until sepsis had settled down and then to amputate, leaving good palmar flaps. The head of the metacarpal bone should not be removed.

Hand surgery should not be undertaken in a big way unless the surgeon was familiar with the complex anatomy of the fascial spaces, tendon sheaths and tendons and nerves. The anatomical spread of infection should be known and some clinical experience gained before any attempt was made to deal radically with infected tendon sheaths and fascial spaces.

The commoner fractures about the wrist should be recognized, especially the fracture of the base of the first metacarpal and fractures of the scaphoid. X ray examination in all doubtful sprains would help in the diagnosis of these cases. It was necessary to remember that small bones did not unite readily, and a long period of correct immobilization was required to produce perfect union. The subject of fractures was too extensive to be dealt with in the present discussion.

Dr. Coates concluded by stating the following simple rules for treatment of injuries of the limbs.

1. Immediate treatment usually means easy treatment and early recovery. There is a "golden period" within the first six hours after trauma—wounds and fractures treated within that period are generally freed from complications.
2. Shock and hæmorrhage should be controlled first.
3. Pain should be relieved; morphine, one-quarter of a grain or even half a grain, should be given if necessary.
4. If violence is adequate, expect an adequate effect. (If a hundredweight of concrete falls on a foot, expect a serious fracture.)
5. Do not disregard persistent or local pain.
6. Use an anæsthetic when necessary; beware of chloroform.
7. Cleanse wounds thoroughly, as in major surgery.
8. Primary suture is never undertaken unless the cleanliness of the incised wound is certain; it should never be undertaken in lacerated wounds.
9. Drain with a rubber dam if necessary; do not drain across tendons.
10. Give tetanus antitoxin in any contaminated wound, and gas gangrene antiserum when the wound is lacerated and dirty.
11. If wounds are infected, never make an incision unless (*a*) local pain, (*b*) local swelling, (*c*) local induration are present. Do not make an incision for red streaks or swollen glands.
12. Do not cut across main lines of structures.
13. Rest, elevation and protective dressings should be used, the last-mentioned being done as seldom as possible.
14. In the provisional reduction of fractured fingers make an X ray examination in all doubtful cases.
15. Regard the hand as the instrument of the brain and treat it with equal consideration.

DR. C. A. M. RENOU discussed traumatic surgery of the head. He said that in introducing the subject of the emergency surgery of head injuries it seemed appropriate to obtain some idea of the type of head injury for which application was made for compensation under the *Workers' Compensation Act*. Dr. Renou proposed therefore to put before the meeting an analysis of one hundred successive and unselected cases in which compensation had been granted for injuries. These figures he had obtained through

the courtesy of the Chamber of Manufactures Insurance Company.

Such claims might be divided arbitrarily into two main groups: (i) Scalp lacerations and contusions. This group consisted of sixty-four cases. The average period of incapacity from work was thirteen days. There were no deaths. (ii) More severe injuries. This group consisted of thirty-six cases in which there were two deaths. Six workers were permanently unfit to resume their former work, whilst twenty-eight returned to work after an average incapacity period of seventy-five days.

Dr. Renou apologized for the small number of cases analysed and stated that for statistical purposes this series was probably of little value. Nevertheless it was interesting to note that the great majority of the injuries were of relatively trivial surgical importance.

Dr. Renou then proceeded to a more detailed account of the various injuries and commenced with a consideration of the minor accidents.

Dealing first of all with scalp wounds (lacerations and contusions), he said that the emergency treatment of this group should always consist in the application of a clean aseptic dressing and the control of hæmorrhage either by pad or bandage pressure, or by the application of a tourniquet around the head, or by digital pressure at some distance from the wound. As soon as these measures had been applied, the patient should be removed to hospital if circumstances permitted. On arrival, provided the patient was not too shocked, an X ray examination of the head might be made prior to the patient's admission to the ward in order to avoid any unnecessary movement at a later stage. The patient was placed in a warm bed and appropriate treatment for shock was instituted without delay.

As these wounds were frequently ingrained with dirt, the sooner excision of the wound edge and damaged tissues was undertaken the better; and if this procedure was carried out it was surprising how seldom gross infection followed. This was probably explained by the rich vascularity of the scalp.

Under local infiltration or general anæsthesia, preferably by gas and oxygen, the floor of the wound was carefully examined for fracture by vision, by the finger and by the probe. A linear fracture usually required no treatment. The management of a depressed fracture would be described later.

Hæmorrhage was controlled by deep catgut ligatures, or by the silkworm gut used for closure of the skin edges. It was wise to drain the corner of the clean excised wound by a rubber dam drain which was left *in situ* for from eighteen to twenty-four hours in order to prevent hæmatoma formation. Dr. Renou considered the best dressing for scalp wounds to be cyanide gauze. In his opinion the use of collodion and similar exclusive dressings was to be deprecated strongly. Their use appeared to increase the liability to infection because they interfered with free drainage. In those cases in which the lacerations appeared to be perfectly clean, as, for example, those due to flying glass from windscreens, it was his practice to attempt primary union by suture without excision of the skin edge. The risk of subsequent suppuration did not appear to be increased thereby.

In concluding consideration of this group of injuries, Dr. Renou stated that an average period of incapacity of thirteen days was reasonably in accord with clinical experience of any superficial wounds adequately treated. In this regard, superficial head injuries differed in no essential fashion from similar injuries in any other situation in the body.

Turning to the consideration of more serious head injuries, Dr. Renou pointed out that different problems arose and were dependent upon injuries peculiar to the brain and nervous system, and so differed from injuries in other situations. In an attempt to demonstrate this aspect of the subject he had analysed all the patients suffering from head injury (243) admitted to the Alfred Hospital during the twelve-month period 1930-1931. From a study of these figures it was apparent that they could be classified into two groups.

The first group included those patients recovered or recovering from unconsciousness at the time of their admission to hospital. In this group there were 148 patients whose average stay in hospital was nine days. Three deaths occurred in this series, two from intracerebral hæmorrhage and one from extradural hæmorrhage. Of the patients in the group, 8% had some type of fracture of the skull. Broadly speaking, the clinical state of the patients in this group could be considered under three headings: (*a*) Those cases in which consciousness was regained and convalescence was uninterrupted, the only after-effect of the injury being a retrograde amnesia for the accident and for a varying period of time preceding it. This characteristic loss of memory was said to be due to the momentary cerebral anæmia produced at the time of the accident. (*b*) Those cases in which consciousness was regained but in which the patient lapsed into secondary unconsciousness with or without localizing signs after a varying period of time—usually several hours. This clinical picture was associated with either extradural or massive subdural hæmorrhage, and operative intervention to relieve compression produced by the clot was undertaken in the majority of cases. (*c*) Those cases in which unconsciousness was not deep and in which recovery was gradual and progressive. These patients all suffered from varying degrees of cerebral contusion.

The second group included those patients who were deeply unconscious at the time of their admission to hospital. In this group there were ninety-five patients. The average stay in hospital of those who recovered was thirty-six days before removal to a convalescent home. There were thirty-one deaths in this series. In all of these fatal cases the patients suffered from some type of extensive intracranial hæmorrhage and over 90% of them showed some form of fracture, most frequently of the base of the skull. The clinical picture was associated with deepening coma and steady depreciation of the patient's condition, death usually occuring within forty-eight hours of admission.

In an attempt to ascertain the ultimate functional results in these head injuries and to determine the frequency of sequelæ arising from actual brain damage, Dr. Renou had written to all the patients in the above two groups who recovered, but only thirty had replied to the *questionnaire*. Of this number eighteen had no after-effects, three suffered from permanent deafness, two were subject to giddy turns, five had attacks of severe headaches, one had lost the sense of smell, one suffered from epilepsy.

Only three of these had been unable to resume their old occupation.

The inadequacy of these figures was shown by the fact that they differed greatly from those of Symons, who stated that of all patients with major cerebral contusions, one-third remained permanently and totally disabled, one-third ultimately were able to resume light work, and only one-third were ever capable of returning to their previous occupation. If Symons's figures could be taken as an accurate indication of the late results of head injuries, these cases presented a serious problem in emergency surgery. It was therefore necessary to consider in some detail this type of case and to decide what methods of treatment were likely to reduce the incapacity period and the development of remote sequelæ.

In all cases removal of the patient to hospital should be expedited, and whilst the arrival of an ambulance was awaited, bleeding should be controlled, a rapid general examination for other injuries should be made, shock should be counteracted by warmth, but the administration of stimulants should be avoided.

On the patient's arrival at the hospital, if the shock was not too great, the skull should be examined by X rays before the patient was transferred to the ward in order to avoid unnecessary movement later.

On admission the patient was placed flat in bed with the head turned to one side, and a period of careful observation was commenced. An accurate history of the injury should be obtained if possible from the patient or, if the patient was unconscious, from witnesses of the accident.

A thorough examination should be made, particular attention being paid to any abnormal neurological findings. During the next six hours the patient's general condition, pulse rate and blood pressure were noted at half-hourly intervals. If any significant change occurred, a further neurological examination should be undertaken. If during this period the patient's condition remained satisfactory the interval of checking was extended to one hour and was continued until consciousness was regained. A chart should be kept of the following details.

1. The depth of unconsciousness. This might be assessed by the following simple tests. Could the patient be roused by vocal stimuli? If not, did he respond to painful stimuli? If not, was the corneal reflex present?
2. The size and relative size of the two pupils.
3. The presence or absence of any difference in muscular power and tone on either side of the face or body.
4. The equality or inequality of the deep and superficial reflexes.
5. The pulse rate and rhythm.
6. The respiration rate.
7. The temperature.
8. The blood pressure.

During this period of observation sedatives should be avoided and a watch should be kept on the bladder to determine whether catheterization was necessary.

Sooner or later an idea of the pathological state which was present would be formed, and an estimate of the amount of brain damage should then be possible.

Dr. Renou went on to state that the conditions which merited consideration might be dealt with under three headings:

1. Fractures of the skull. Those which called for special treatment were compound fractures of the vault and depressed fractures. Each type was an indication for operation, and in the former class urgent operation to excise contaminated tissues and so to minimize the possibility of infection. When a depresson exsted, the object of operation was not only to elevate the depressed bone, but also to remove loose and possibly soiled fragments and to provide external drainage. One of the most common causes of traumatic epilepsy was cortical laceration with subsequent scarring; therefore the importance of the removal of indriven bony spicules was evident. If the depression was pond-shaped and the fracture simple, non-operative treatment resulted in little permanent harm. After removal of loose and depressed bony fragments the *dura mater* should be carefully inspected. If undamaged, it should not be opened, but if torn the damaged edges should be excised, lacerated brain and foreign material should be removed by suction and gentle irrigation with warm saline solution, bleeding should be arrested and the wound should then be closed with drainage.

2. Vascular injuries. Neurological signs either of a focal character or indicative of increasing generalized compression, when superimposed on the clinical picture produced by the head injury, were of the greatest importance, because they so frequently indicated intracranial hæmorrhage calling for surgical intervention.

The time relation of the onset of symptoms of compression to the accident, and their subsequent rate of progress, often served as indications of the underlying pathological condition. (*a*) If there was no lucid interval and compression occurred early and was rapidly progressive, the cause was usually extensive subarachnoid or intracerebral hæmorrhage, and little could be done surgically. (*b*) If the lucid interval commenced several hours after the accident and lasted for several hours before the onset of compression, the cause was usually a middle meningeal hæmorrhage. (*c*) When the lucid interval was of some days' or weeks' duration the localizing signs accompanying the compression were frequently bilateral. In this instance the cause was usually a subdural hæmatoma, often arising from a torn cerebral vein as it entered the sagittal sinus. These last two groups of hæmorrhage called for urgent surgical intervention.

The side of the head to be explored was often determined by the presence of a contralateral hemiplegia. This was confirmed if an ipsilateral, widely dilated pupil was present; but the surgeon should not hesitate to explore the opposite side of the head if no blood clot was found on the side first explored.

Referring to local anæsthesia, Dr. Renou said that a 1% solution of "Novocain" was the anæsthetic of choice. He considered that the best incision was a straight vertical one, one inch in front of the ear in the temporal fossa, splitting the temporal muscle. The temporal bone was trephined, and if a middle meningeal hæmorrhage was present the clot was at once seen, the bone opening was enlarged with nibbling forceps and the clot was removed. The bleeding vessel was searched for and ligated, or if the vessel was in a bony canal the canal was plugged with a sterile match stick or bone wax.

If no epidural hæmorrhage was found, a bluish tinge of the dura would indicate an underlying hæmatoma. The *dura mater* was incised and the clot was turned out. It might be necessary to make a second small incision in the dura further back in the parietal area to facilitate removal of the clot by syringing through from one to the other. A small osteoplastic flap might on occasions be more suitable than this approach when dealing with this type of hæmorrhage. Large osteoplastic flaps were contraindicated and were seldom necessary in traumatic surgery.

3. Brain contusions and lacerations. Patients suffering from uncomplicated contusion and laceration required immediate physical and mental rest. They should if possible be placed in a quiet and darkened room. In order to check the reactionary œdema which followed the brain injury, continuous dehydration should be carried out by a six-hourly introduction *per rectum* of six ounces of a 50% solution of magnesium sulphate. The fluid should be warmed and inserted by funnel and tube. To produce the maximum effect the solution should be retained for half an hour.

Lumbar puncture was not necessary as a routine procedure, but if unconsciousness persisted for thirty-six hours it should be carried out and the cerebro-spinal fluid pressure was then measured by manometer. The colour of the fluid obtained would indicate whether bleeding had occurred into the subarachnoid space. If the pressure was above 120 millimetres of water, fluid should be run off until this level was reached. Intravenous injections of hypertonic solutions (of which 50% glucose was the best) should not be used unless the cerebro-spinal fluid pressure remained persistently above 200 millimetres of water. These solutions were most valuable as dehydrating agents, but if localized intracranial clot was present their use involved considerable risk, as the resulting rapid dehydration might produce further bleeding. Again, they were on occasions the cause of acute pulmonary œdema.

When consciousness was regained, headache, lack of concentration, insomnia, or giddiness on movement might continue for a varying period, during which absolute rest in bed must be insisted upon. Potassium bromide and chloral hydrate given three times per day would be most beneficial and "Luminal" in half-grain doses often relieved the giddiness considerably.

When free from symptoms for forty-eight hours, the patient might be allowed out of bed for short periods each day. If he remained well for the ensuing forty-eight hours he might then be allowed short walks. If he remained well for a further forty-eight hours he might resume a normal life at home, and after another forty-eight hours he should be sent away for a quiet holiday in the country for at least a fortnight before he resumed his normal work. Any return of symptoms during this period of convalescence was an indication for a return to the stage at which the patient was previously symptom-free.

In conclusion, if this routine was followed the average patient would be fit to resume his work in about one month from the time of injury, but there would be many cases in which convalescence was prolonged and might last for several months. The type of work to which the patient was to return had to be considered, and it was important that he should be tested as fully as possible before he was declared thoroughly recovered. If the initial unconsciousness was longer than forty-eight hours bromides should

be taken each night for the ensuing two years as a preventive against epilepsy.

DR. ERIC HUGHES-JONES, who dealt with injuries to the trunk, began by stating that he was deeply indebted to the Workers' Compensation Reports of New South Wales and to the opinions of Dr. Mackay, the chief medical referee of the Commission, so ably set out in the annual reports of the Commission.

In 1936 the Workers' Compensation Fund compensated nearly 44,000 men for injuries; 3,500 of these received injuries to the back, of which nearly 3,000 were sprains and strains, and the remainder superficial bruises; 1,300 men received rib injuries, either bruises, fractures or sprains. Of the 480 who received abdominal injuries, 340 suffered strains and sprains and 100 bruises; 350 men were compensated for hernia.

Dealing first with injuries to the back, Dr. Hughes-Jones said that Steindler and others thought that two-thirds of the cases of sprains and strains of the back were concerned with injury to the lumbo-sacral and sacro-iliac joints—they were at the junction of the movable and fixed portions of the skeleton. It was the duty of general practitioners who would see these patients to make themselves familiar with the features of lumbo-sacral and sacro-iliac strain, lesions which produced definite physical signs and concerning which manipulative tests gave concrete evidence. These lesions had recently been discussed fully by Littlejohn at the congress in Adelaide and the special tests could be found by reference to the works of Smith-Petersen and Steindler. Radiological examination did not help in the diagnosis of these conditions, although it was necessary to ensure that a fracture was not present. The removal of infection from the mouth was a necessary part of the management of these patients.

In the majority of back injuries, skiagrams showed some degree of spondylitis, usually early. Even pronounced osteoarthritic changes apparently might not affect the worker's capacity, though if he was aware of the fact it might affect him subjectively. *Spondylitis deformans* might often be present and cause no disability to the worker. Undoubtedly injury aggravated the condition and the back sprain which should in a normal case clear up in a few weeks tended to develop into a "chronic back". The willing man carried on and his condition improved. To others the name suggested a very serious state and the workman treated himself as an invalid. Bony changes in the vertebral bodies and the intervertebral disks might lead to serious permanent disability.

Failure to try to work might be the cause of continued incapacity for work. In one instance a decision had been given that the cause of unfitness for employment was nothing but the man's long-continued and unnecessary idleness, he not having worked for three years. When a workman was fit for light work preparatory to a return to full work it was usually considered that there was need for a period of rehabilitation of three months to enable the worker to tone up his musculature to fit him for the work that he had carried out before his injury.

Mental obsession following injury to the back was so difficult to overcome that every care had to be taken to prevent an obsession from arising. Tactful handling from the first, firm management, expression of opinion on definite clinical evidence only, avoidance of mention to the patient of high-sounding names of diseases, avoidance of the application of impressive but unnecessary supporting apparatus—observance of these might conduct the patient along a normal course.

Discussing hernia, Dr. Hughes-Jones said that they were not concerned with the development of the hernial sac, but they envisaged the appearance of the hernia. The mechanism of the inguinal canal was a nice provision for security at a moment of expected effort; for in the preparation of the abdominal muscles to meet the strain the lower edges of these muscles approached the inguinal ligament and prevented the escape of omentum or bowel even in the most likely circumstance, the presence of a patent *processus vaginalis testis*. But sometimes at work the strain fell on the abdominal muscles unexpectedly, the foot slipping or the weight dropping into the hands, and the inguinal canal was not protected in time, so the omentum or bowel entered the patent processus and forcibly distended the sac and its internal opening. This would be accompanied by pain, the workman would complain to his foreman or his fellows, he would be unable to carry on with his heavy work, and he would probably notice a lump and see his doctor that day or the next. These were some of the criteria which enabled the medical attendant and the medical referee to decide whether that particular man had a compensable hernia. A concise and clear-cut history would carry its own conviction.

In a normal person a direct inguinal hernia as a result of exertion was unlikely to occur, but it might occur from direct violence to the abdomen in those in whom the muscles were of poor tone.

Dr. Hughes-Jones then referred to torsion of the testis. He said that Muschat held that torsion of the normally developed testis and epididymus was exceedingly rare, but he was convinced that torsion did occur in that uncommon error of development in which there was high investment of the testis and adnexa by the tunica; in other words, the testis was freely movable, free of any lateral attachments and suspended in the vaginal sac by a long stalk of spermatic cord. Muschat had operated in such a case and had found the intravaginal portion of the spermatic cord firmly twisted, and he believed from a study of recorded cases that this condition was present in all. The result of the torsion was immediate incapacity for work, and at operation the twisting of the cord was unmistakable.

Dr. Hughes-Jones concluded by saying that a new social problem had been created in medical relations by the financial provisions of recent amendments to the *Workers' Compensation Act* of Victoria. It seemed that the care of many workmen would pass from the public hospitals to the general practitioner, and it was of the first importance that the conduct of the medical care should be wise.

PROFESSOR R. MARSHALL ALLAN introduced Professor G. Grey Turner as a distinguished visitor from England whose erudition and philosophical address with many apt quotations had delighted a large audience at the opening of the Post-Graduate Surgical School on the previous day. Professor Grey Turner had been the President of the Section of Surgery at the Adelaide congress and was the head of a great post-graduate medical school in London. It was of interest to note that the Victorian Branch of the British Medical Association many years earlier had started the first post-graduate organization. As President of the Branch he had much pleasure in welcoming Professor Grey Turner to Melbourne and to Victoria and he asked him to open the discussion.

PROFESSOR GREY TURNER said that he had been delighted with the activities of the British Medical Association in Australia and in Melbourne and he was sure that great value arose from the meetings. He had come in a little late and had gathered from the papers that the subject under discussion was the problems in compensation arising from traumatic emergencies affecting the various regions of the body. At the outset he had been delighted to hear Dr. Coates urging that medical practitioners should not be punctilious about suturing wounds of the hand; he was in entire agreement. Particularly in injuries of the hand and in minor injuries in general harm was done by concentrating thought on the ultimate appearance of the scar without taking into account the danger of locking in sepsis. He was disappointed that he had not heard about bismuth, iodoform and paraffin paste ("B.I.P.P."), which was associated with the name of his great colleague Rutherford Morrison, who had introduced this paste for use in traumatic surgery during the Great War; it had a special value, too, in the injuries of industry to save too great a sacrifice of tissues in excision operations. One part of bismuth should be used with two parts of iodoform. It was Professor Grey Turner's practice to use this combination as a powder ready mixed or made up with carbolic acid solution (one part in forty parts of water) rather than in paraffin, and he thought that it was equally valuable. It should be remembered that "B.I.P.P." interfered with proper radiographic examination on account of

shadows. Another omission was the value of the simple method of grafting a whole skin thickness which was known as the Wolff graft.

The remarks about such foreign bodies as needles made by Dr. Coates were regarded by Professor Grey Turner as wise. He had seen many disasters resulting from ill-considered efforts in out-patients' departments; unless the foreign body could be felt no attempt should be made to remove it without localization. In cases of difficulty he drew attention to the extreme importance of collaboration between the surgeon and the radiographer and also affirmed that a general anæsthetic should always be administered. If sepsis was introduced a hand might be spoilt by it rather than by the presence of the foreign body; the removal should be a major operation with an anæsthetic and adequate time should be spent by the surgeon and skilled assistance should be provided as in other major operations.

In injuries to the terminal phalanges with necrosis of bone Professor Grey Turner pointed out that sequestra separated readily and in great majority of cases would be discharged from the wound; a formal operation was usually not necessary and in his opinion should not be performed. With reference to cut tendons, he was aware that there was a school which thought it better not to attempt suture at the first operation, but to perform a secondary operation for this purpose after healing had occurred; he was not convinced, however, that this was the best practice. In any case, tendon suturing should be regarded as a job for a specialist and adequate assistance and a suitable theatre environment were requisite. It was not safe to suture a cut flexor tendon and expect or urge the patient to use it in three or four weeks; irrespective of the findings of animal experimentalists, it took double or treble this time in human beings. It was necessary to wait until the patient could move the part without pain or discomfort, and he should not be urged to move the part nor should manipulation be undertaken prematurely.

Professor Grey Turner said that he was interested in the figures in the paper on head injuries by Dr. Renou; wages must be good in Australia if it was possible to get the workers with minor head injuries back to work in so short a period as thirteen days. In serious cases, even though there were no symptoms, it should be assumed that the brain had been seriously perturbed and that a long period of convalescence was necessary to prevent sequelæ. Mr. Symons, of Guy's Hospital, had been quoted by Dr. Renou; he was a son of Sir Charteris Symons and was a very careful worker whose figures could be relied upon. Professor Grey Turner went on to say that there came a stage in convalescence from head injuries when undoubtedly the patients should be under discipline of graduated work; it was so hard to fill in the gap between absolute disablement and ability to perform the ordinary avocation; the question of the provision of light labour should be taken cognizance of by the insurance companies; it was unfair to send the worker back to his work too soon and it was frequently difficult to provide him temporarily with light work. It was wise to remember that gross changes previously present might be lit up with the symptoms at the time of an accident and the remarks about the use of long names in front of the patients in discussions were apt and important; ideas arising out of them in the mind of the patient were liable to complicate the problem of the complete restoration and return to normal work. Professor Grey Turner used the reference to torsion of the testis as an example of a question which could be settled as to the facts by research work not demanding any provision of laboratory facilities or other incidental items of expense. He had always thought that torsion could occur in the fully developed normal testis. The matter of accident as a cause of hernia was an important one; the fine work of the late Hamilton Russell, of Melbourne, had guided surgeons in England and elsewhere; they were indebted to him and most of them agreed with his views about the conversion of a potential hernia into an actual one by an act of violence. The onus of proof that the accident was causative depended on the patient; if the occurrence of the accident was proved and the collateral circumstances supported the statement of a dependable patient known to the medical examiner, it was usual to allow the claim.

With further reference to the paper by Dr. Hughes-Jones, Professor Grey Turner stated that under the industrial insurance scheme operating in Great Britain it had been decided in recent years that it was necessary for the practitioners to keep clinical notes about their patients' ailments; records were of great value for the protection of the doctor as well as the benefit of the patient. If a patient had some injury that would not ordinarily require radiographic investigation, but the surgeon thought it advisable in the special circumstances of an accident, the patient might refuse it or put obstacles in the way; Professor Grey Turner considered that in such a case a junior practitioner particularly should protect himself by writing a letter to the person responsible reiterating the advice and retaining a copy as evidence that he had given such advice; by these means unpleasant situations in courts of law would be abolished.

PROFESSOR MARSHALL ALLAN thanked Professor Grey Turner and introduced Sir Henry Newland, who had been the President at the Adelaide congress, and who had received the gold medal of the British Medical Association in Australia in recognition of his eminent services to the Association. Professor Marshall Allan took this early opportunity of congratulating Sir Henry Newland on behalf of the Victorian Branch and said that the session of congress had been very successful. He invited Sir Henry Newland to contribute to the discussion.

SIR HENRY NEWLAND thanked the President of the Victorian Branch for his congratulatory remarks and attributed the success of the congress to the work of the able committees. The weather had been wonderful and the South Australians had appreciated the size of the attendance from the other States. The papers were of a high quality and the discussions excellent.

He was entirely in agreement with everything that had been said by Professor Grey Turner. In a discussion on compensation for accidents stress had to be laid no doubt in a great proportion of instances on the disabilities extraneous to the actual injuries. Close contact should be kept up between the patient and the practitioner. If doubt existed the patients drifted into neurotic conditions. For instance, if a man was injured on the docks and was attended by a lodge doctor or at a hospital out-patients' department and was seen only twice a week, he might not get that continuous attention which ensured quick results. It would be wise to establish hospitals for traumatic surgery in large centres as had been done in the United States of America. Insurance companies should realize the benefits of this scheme.

Sir Henry Newland expressed the opinion that the more experience one had with needles in the hand the less secure one felt about the prospect of removing them easily; rarely was the procedure satisfactory with local anæsthesia and he agreed that general anæsthesia should always be used. Speaking of care in the use of tourniquets, he stated that the tourniquet should not be kept on too long or employed wrongly; rubber tubes should not be of insufficient diameter and the limb should always be protected. He considered that the blood pressure apparatus was the safest type of tourniquet to use.

In spinal injuries radiography sometimes revealed the presence of an actual condition that had been in existence for years. If this preexisting condition was impressed on the mind of the patient, disability was liable to be prolonged by processes which were mental in origin. He had noticed that these disabilities did not occur in footballers or other people who were wrapped up in their occupations. It was quite exceptional to see post-traumatic neuroses in jockeys, for instance, who, as a class, were eager to get back and ride again as soon as possible.

DR. JOHN KENNEDY strongly endorsed all that Dr. Coates had said about the treatment of a worker's hands. From some of the results that had come under his notice it might be supposed that Scudder had never lived. Fractures and

dislocations should be reduced absolutely; after reduction the position could not be maintained by means of straight splints. He mentioned a demonstration by Dr. Glissan of the use of aluminium sheeting, a pair of shears and a hammer, by means of which any splint for the hand could be fashioned on the spot; these splints when well made were much easier and cleaner to use than was plaster of Paris. He exhorted practitioners to remember the tendon sheaths and not to treat lightly even minor injuries about the thumb and index fingers. In cleaning up wounds of the hands he asked that lotions, such as lysol, carbolic acid and picric acid, should not be used; even a 2% solution of picric acid could produce a dermatitis which prolonged invalidity enormously, and the other lotions had been known to cause gangrene of the fingers. Dr. Kennedy did not think that Dr. Coates had been sufficiently explicit about the question of amputations of parts of fingers; any part that could be left should be left, as it was of such great use to man. In all circumstances Dr. Kennedy opposed the removal of a proximal phalanx or the head of a metacarpal bone.

With reference to what Dr. Hughes-Jones had said about the "low back" patients, Dr. Kennedy commended to the attention of all members the very clear exposition of the diagnosis and treatment which had been given by Dr. C. W. B. Littlejohn in Adelaide in the previous week. Sir Robert Jones had laid it down that the essential in the treatment of low back strain was fixation and he had described the use of brown paper soaked in glue, the brown paper being brought well round the abdominal wall. Nowadays a similar effect could be obtained by the use of strapping, and the disability period averaged eight weeks. If the treatment adopted was to put the patient at rest in bed and use diathermy the period would be prolonged probably to nine months. Speaking of the diagnosis of hernia arising out of an accident, Dr. Kennedy stated that it was necessary that there should have been an accident and that the patient should have told the foreman and that he had sufficient real pain and swelling to go to see a doctor. If these points were established to the satisfaction of the company's referee the claim would be allowed. It was recognized in insurance circles that head injuries resulted in serious disability. In the last twenty cases that had come under his notice in only some had the disability period been less than a few months. He related the case of a man who had been admitted in an unconscious state to a public hospital in Melbourne after an accident in which the skull had been fractured. After one month he had been discharged from hospital, but was arrested on the doorstep and spent the next two months in the gaol hospital. Three months after the injury he went to work as a lorry driver and nothing had happened. Dr. Kennedy considered that there had been too much haste in getting these patients out of hospital; a long rest was necessary until the brain damage had entirely cleared up. A long period of disability and serious sequelæ could be avoided by this means.

DR. THOMAS KING said that in the class of work under consideration the hand was the outstanding portion. Primary excision of the wound should be attempted within six hours of the injury if the patient presented himself in time. He should be admitted to hospital if the injury was at all severe. Proper treatment should be carried out in an operation theatre. At Saint Vincent's Hospital this early excision was practised; the arm was placed in abduction and immobilized in plaster of Paris if necessary. Loose suturing was performed; the wounds were not left entirely open; when the wound was infected, of course, there must be free drainage. The question of splinting was another important matter. Dr. King was very opposed to the use of hot foments or the prolonged soaking in lotions of an injured limb. He considered that guillotine wounds should be closed up; the bone was more liable to osteomyelitis if the wound was left open. Traumatized tissues should be excised and the wound disinfected; it was then safe and proper to close it.

Dr. King considered that the repair of injured hand tendons in general was a secondary operation to be performed three weeks after the healing of a clean wound, six weeks after the healing of a contused wound, and two to three months after sound healing of a suppurating one. The counter-irritation test with radiant heat and other tests should be applied first. The primary operation could be considered appropriate only when the best conditions prevailed: (*a*) when the wound was a clean section with a clean razor, sharp knife or glass and was not lacerated, contused or contaminated; (*b*) when the surgeon was experienced and skilled assistance, a suitable operating theatre and correct instruments were available. Dr. King emphasized the point that primary suture should not be performed more than three to six hours after the accident. In certain situations he stated that primary suture was often practicable. These situations were: (*a*) the extensor tendon, especially on the dorsum of the metacarpus, though here it was often unnecessary on account of the presence of the *junctura tendinum*; (*b*) the flexor tendons near the wrist. Primary suture was seldom justifiable or successful in the osteofibrous canals of the fingers. These wounds should be excised, the sutured fingers splinted, the limb placed on an abduction splint, and as a rule the patient should be admitted to hospital. If all went well, some weeks later the repair operation should be undertaken. Dr. King mentioned that he had had numerous successes. He preferred to use a pneumatic tourniquet rather than a piece of rubber tubing. After applying the tourniquet he made a relatively long incision and did a quick and rough operation, avoiding only nerves and blood vessels. He removed any frayed portions of the tendon and did not use tendon grafts. He was content to suture the profundis tendon and to ignore the sublimis tendon. He ended by meticulous sewing, and at the end of the operation the tip of the finger rested almost on the palm. He attributed what success he had had to the early movement which was involuntarily attempted by the patient and to the gradual stretching that followed as the patient learned slowly to move the finger away from the palm.

Dr. King agreed with what had been said about the removal of needles, but he wondered whether it was always necessary to remove such foreign bodies. If it was shown radiographically that the needle was in a place where it would not do any harm he thought that there was no need to operate.

DR. J. B. COLQUHOUN expressed his great delight in listening to the papers. In the main there was very little with which he could disagree. It was not uncommon for patients to get paralysis after the use of a tourniquet on the superior extremity. He did not consider it was essential to use a pneumatic tourniquet. The proper application of rubber tubing was difficult; the person applying it was liable to use too much strength rather than too little. He liked to use the inner-tube of an ordinary bicycle tire (which was twenty-eight inches by one and a half inches); when cut in two this tube could be applied at any tension desired, could be sterilized, no padding was necessary, and paralysis was rare if it ever happened. Dr. Colquhoun preferred to deal with tendons almost immediately after the accident and when they had been cut cleanly by a sharp instrument or a piece of glass, but the suturing should be attempted only by those who were used to it and expert at it. He agreed with the conservative attitude that Dr. Coates had adopted about amputations of portions of fingers. Dowden, of Edinburgh, taught that the tendon should be sutured securely to get minimal contraction and to educate it to glide in its sheath. There was no need to bring anyone to Melbourne to show how to cut aluminium splints; they were very good, but there were more ways of killing a dog than by hitting it over the head with a stick.

Dr. Colquhoun asked Dr. Renou, whose greater experience in head injuries he acknowledged, whether chips of bone should be removed and washed and put back or whether they should be thrown into the bucket. Speaking of the "low back" problem, Dr. Colquhoun suggested that the habit of telling these people to come back next week and the period of waiting set up the mental process from

which traumatic neurosis arose. No man without special experience should attempt the treatment of lumbo-sacral and sacro-iliac disabilities. Smith-Petersen had described a system of examination of these patients which included exact methods of diagnosis and treatment. Anyone trained in the methods could follow them and treat his patients intelligently. It was quite wrong to talk learnedly about these things in the hearing of the patient. Even what appeared to be an example of sacralization in the stereoscopic film might not be so after all. The principle of treatment was to immobilize the patient until he got rid of the pain and to show an intelligent interest in him and to pay close attention to his condition. In this way neurosis would be eliminated and there would not be so many malingerers wandering about the out-patient department. This practice had been introduced forty years previously in Massachusetts by Joel Goldthwait. At that time 75% of the women with backache were referred to gynæcologists but nowadays only 10% were sent to them. The gynæcologists should be grateful to the orthopædic surgeons.

DR. H. F. MAUDSLEY made a plea for personal observation of the patient from the outset. Dr. Colquhoun had stressed this point in connexion with the lesions of the back. Dr. Maudsley considered that 70% of traumatic neuroses could be nipped in the bud. Neurologists and psychiatrists did not see the patients until much later and until extraneous events had occurred. He considered the question of radiography extraordinarily important; certainly the appearances should not be discussed with the patient. A man might have a mild injury to the head and at inspection of the skiagram some mild abnormality of the skull might be seen and regarded as evidence of a fracture. Although on consideration the doctors decided quite definitely that no fracture was present, some patients would not accept this verdict, but months and months later were still receiving insurance money each week. Dr. Maudsley added that most of them got better even at the late stage at which they saw the psychiatrist, but at times there was some real underlying cause for the protracted invalidity. He instanced the case of a jockey with narcolepsy which had been regarded as neurosis for some years. It should be remembered, too, that a worker such as a dock labourer was in a continual state of conflict. If he gave up the compensation and applied for the old class of work, admitting that he had had a head injury or a back injury, he was liable to be "landed in the soup" by a refusal of reengagement; this state of conflict engendered neurosis.

DR. W. W. OSTERMEYER referred to the medico-legal aspect of traumatic emergency surgery. He would not like to hear it said in front of a jury that a piece of needle in a person's hand should not be removed. Members of the jury would think that it might perforate a blood vessel and it was difficult to convince these people that pieces of glass were not likely to travel. He mentioned a woman who had lost a needle and six months later it was found that she had sat on it; although this needle was in soft tissues it had not moved.

PROFESSOR MARSHALL ALLAN commended to the notice of those present the desirability of coming to a decision about the advisability of the establishment in the suburbs and in the metropolis of traumatic emergency centres, with hospital accommodation fitted with facilities for the treatment of industrial injuries and serviced by means of a duty roster, to keep the treatment of these patients in the hands of private practitioners.

He called on those who had read the opening papers to reply briefly to any controversial points that had been raised in the discussion.

Dr. Coates said that "B.I.P.P." had continued to be used at the Royal Melbourne Hospital until about four or five years earlier. Because of the occurrence in a few odd cases of iodoform rashes it had been given up and milder and less dangerous antiseptics were used. He was in agreement that six weeks should be a minimal period of immobilization of a sutured flexor tendon of the wrist or hand. He had not seen a case in which a perfect result had followed the suturing of the flexor tendon distal to the metacarpo-phalangeal joints; in some instances partial movement had been obtained.

Dr. Coates thanked Professor Grey Turner and Sir Henry Newland for their valuable contributions to the discussion, but he was sorry that Sir Henry Newland, who was a recognized world authority on skin grafts, had not said anything about them that night. He also thanked Dr. John Kennedy for his remarks. He represented the views of the insurance companies. Dr. Coates still felt, in spite of what Dr. Kennedy had said, that when suppurative teno-synovitis ensued in a septic traumatic crushing wound, the decision as to the site of amputation had to be made in each case on the merits, and at times one might have to amputate at the metacarpo-phalangeal joint. It was his custom, however, to teach and to practise that every piece of finger that could be retained should be retained; one might get surprisingly good results at times if the patient would move the small joints as had been taught by Willems. Under present conditions a large proportion of the traumatic emergency surgery was in the hands of general practitioners, who should make it their business to apply sound principles, treat the patients intelligently, and realize their own limitations. Dr. King's ideals concerning the value of early treatment might be attainable if traumatic hospitals were numerous and well equipped in various parts of the city and country.

Dr. Renou said that the only question that had been raised arising out of his paper was the inquiry from Dr. Colquhoun about the comminuted fragments. He remembered that, when he had been assisting Dr. A. J. Trinca at an operation on a publican who had been hit on the head, Dr. Trinca had washed the pieces and put them back again. A good result had followed, and from that time Dr Renou had adopted a similar procedure and had not regretted it.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held on Wednesday, July 14, 1937, at the Children's Hospital, Carlton, Melbourne, DR. ROBERT SOUTHBY, the President, in the chair. The meeting took the form of a number of clinical demonstrations followed by a discussion by the members of the Society. Part of this report was published in the issue of December 11, 1937.

Multiple Infective Synovitis.

DR. ERIC E. PRICE showed a girl, aged twelve years and six months, who had first come under observation on February 16, 1934, on account of a warm swelling of the left ankle, causing very little pain either at rest or on movement. It was found that the reaction to the Mantoux test was positive, but the radiographic films were of normal appearance. The condition was regarded as a non-specific infection, and the leg was put in plaster for four months. The condition had subsided, but even a year later some thickening was noticeable behind the malleoli. When the patient was again seen on December 18, 1935, the right ankle and knee and the left elbow had become sore. The exacerbation subsided in less than one month. A blood sedimentation rate curve during this period was of the active type. The patient reported again on September 30, 1936, with pain in the right knee and in the little fingers. There was a slack effusion in each knee, but little was found to be wrong with the fingers. The condition was practically painless, and the general health seemed excellent. At that time the patient's serum had failed to react to the Wassermann test, and no bony changes could

be identified radiographically. The blood sedimentation rate curve revealed a fall of 20 millimetres in one hour. The fluid removed from the knee joints was examined and attempts at culture were made. It was sterile fluid, but there were many cells present in it: polymorphonuclear cells numbered 31%, large lymphocytes numbered 42% and small lymphocytes numbered 27%. At that time the patient had received dental attention, and the tonsils and adenoids were removed. Though she was at rest in bed, the effusion persisted; and while she was in the ward from January 6 to January 23, 1937, a dental vaccine of non-hæmolytic streptococci was prepared. The blood sedimentation rate showed a fall of 14 millimetres in one hour.

On February 24, 1937, she was transferred to the Frankston Orthopædic Branch and was treated for a while with the vaccine and later with injections of "Aurasol". The activity of the condition had subsided for four months, though there had been a considerable variation in the amount of effusion. For ten weeks before the meeting there had been no demonstrable effusion. On April 6, 1937, pyuria had been noticed for the first time. Culture of the urine resulted in the very slow growth of Gram-positive diplococci. By excretion pyelography Dr. Price had demonstrated a pelvic hydronephrosis and hydroureter on the right side, the shadow lagging five minutes behind that of the left side, which was normal. By cystoscopy he had seen that the bladder mucosa and left ureteric orifice were normal, but that the right ureteric orifice was patulous and crenated in outline, and that it appeared to be œdematous and inflamed. Urine from the left kidney was sterile. Retrograde pyelograms had confirmed the existence of pelvic hydronephrosis and hydroureter on the right side, and it could be seen that the ureter was not implanted into the lowest part of the pelvis. The lower calyces were not visible, but it was probable that they were obscured by the abnormal shadows. The bladder appeared to have a normal capacity, but there was not any vesico-ureteral reflux even with pressure and posturing. The capacity of the bladder was approximately twelve ounces, and there was less than one ounce of residual urine.

Dr. Price said that, at the time of the meeting, no physical signs of pathological significance could be elicited. The joints had become normal in appearance, and the blood sedimentation rate gave a fall of only four millimetres in one hour. The affected kidney was not palpable. The multiple joint infections and the idiopathic hydronephrosis and hydroureter had been of interest in the case.

Dr. Price said that the dilatation of the urinary tract met with in children fell into four anatomical groups. (i) Dilatation of the pelvis only: this might be of the pelvic or renal type of hydronephrosis, and was frequently bilateral, though not of the same degree on each side; it might be confined to one portion of a kidney in a patient with bifid ureter. (ii) Dilatation of the pelvis and ureter: this was also common, and might be bilateral, though not equally developed. The ureteric orifice was usually found to be dilated and patulous, with no evidence of obstruction, and the phenomenon of vesico-ureteric reflux might be shown, but was not constant. The significance of this reflux was not known; Oberneidermyer had shown that it occurred constantly in the rabbit under deep anæsthesia. (iii) Dilatation of the pelvis, the ureter and the bladder: in these cases the condition was always bilateral, and the bladder showed hypertrophy and trabeculation, with increased capacity and residual urine. It occurred in males and females. (iv) Dilatation of the pelvis, the ureter, the bladder and the colon: Aird had reported that 5% of the cases of Hirschsprung's disease were associated with hydroureter.

Dr. Price said that examples of the first three types were to be found in the Children's Hospital pathological museum. He thought that the problem of treatment depended on the conception one had of the ætiology, but this was very obscure. Infection probably played a part, but in these idiopathic cases it was probably secondary. There were two schools of thought, the mechanical and the neuro-muscular schools. According to the mechanical school, various obstructing lesions had been noted, and were thought to be the essential factor, varying with the anatomical type. In the pelvic type there had been found aberrant arteries, congenital and inflammatory strictures of the pelvi-ureteric junction (Winsting White), high origin of the ureter and congenital flap valve formation. Strictures of the lower end of the ureter had been noted, and Young had described a flap valve formation in the prostatic urethra. When no obstruction could be demonstrated, it had been suggested that the valve was "one way" in action.

The neuro-muscular school postulated that there had been a functional failure, either of the whole involved tract or of its lowest segment, to facilitate the expulsion of the urine. It would be of the nature of a spasm or an achalasia. Dr. Price said that there was some positive evidence for this; first, the occurrence of cases in the absence of any obstruction, no abnormality being revealed *post mortem*; secondly, the association with Hirschsprung's disease, which had been influenced by denervation operations; thirdly, the examination of patients with a reflux, when obstruction, either mechanical or functional, was absent. This suggested that the primary failure was not so much a passive dilatation in the face of obstruction as a diffuse failure of the urinary tract to keep small. Dr. Price pointed out that a closer analysis of the neuro-muscular defect was at present impossible. It was generally conceded that the ureter was innervated entirely from its distal end by sympathetic and parasympathetic fibres derived from the hypogastric plexus. The renal plexus might contribute to the upper end, but he thought it improbable that any fibres entered along the course of the ureter. Dr. Price thought that in this way it should be possible to interrupt both systems by dividing the ureter and reimplanting it in the bladder, or to interrupt the sympathetic system only, by a presacral operation. Unfortunately, the effect of section did not seem to have been sufficiently studied. Dr. Price said that in treatment, when one kidney was hopelessly damaged and the other was completely normal, nephrectomy offered an easy solution; but commonly the other kidney showed evidence of disease, which could be expected to progress. On the other hand, as in the patient shown at the meeting, the affected kidney was too good to sacrifice; infection was slight and dilatation was small.

Dr. Price remarked that in the early cases, before secondary changes in the visceral walls had occurred, which made a return to normal impossible, it seemed very desirable to develop some conservative method of treatment. Clinical reports on the effect of presacral neurectomy and on ureteric implantation varied, and it was with the idea of provoking discussion on these lines that Dr. Price had shown the patient.

DR. WILFRED FORSTER said that he had frequently seen older patients with double hydronephrosis and pyuria resulting from a recent abscess on one side. If progressive dilatation of the kidney pelvis was occurring and if pus was still coming down, the wise plan was to remove the kidney. If the focus of infection was in one kidney tract, the other would certainly become infected, and the condition would then be most troublesome.

DR. D. O. BROWN said that the subject of hydroureters was of great interest. He thought that pyelograms should be made in the case of all patients with persistent pyuria. He had not been able to find anything definite and certain about the nervous mechanism of the ureters; further help from neurologists was required. He thought that three different types of hydroureter could be described. In the first type, a definite stricture was to be found in the intramural portion of the ureter. In the second type, there was tremendous dilatation of the whole of one or both ureters, with some contraction at the end, and hypertrophied longitudinal muscle was demonstrable. In the third type, a grossly dilated, widely open, pouting ureteric orifice was present, and fluids could be run into the ureter from the bladder by means of posturing. This type was usually associated with dilatation of the bladder; Young, of Baltimore, had written a lot about it. A chronic urethral valve-like obstruction was found at times, and was

postulated as an explanation of the condition. R. O. Ward, of Saint Bartholomew's Hospital, some four years previously had performed presacral neurectomy with a brilliant result in the only patient so treated that Dr. Brown had seen in the medical literature. The condition was unilateral, dilatation was not gross, and very little infection was present in the case of Dr. Price's patient, and presacral neurectomy might be expected to improve his condition. It would be worth while to communicate with Ward, to see if his patient was still in a satisfactory state of health four years after the operation.

DR. GRAEME ROBERTSON was asked to express his views on the subject. He said that he found it somewhat embarrassing to do so, as the literature was rather complicated and there was no adequate neurological explanation. He thought that a factor which had not been mentioned was the mechanical factor of kinking of the ureter.

Osteogenic Sarcoma.

DR. REGINALD WEBSTER reviewed the case history and exhibited specimens relating to a girl, aged eleven years, who had recently died of osteogenic sarcoma. She was admitted to the Children's Hospital on February 17, 1937, with a note from her outside medical attendant, in which it was stated that one month previously she had sustained a slight injury to the left knee. For the ensuing three or four days she had limped and complained of slight aching pain in the knee. One week after the injury swelling appeared in the distal end of the left femur and, the swelling progressing, it was considered advisable to take a radiogram.

The radiologist reported the presence of a gross destructive process in the distal end of the diaphysis of the left femur, involving the entire width of the bone except for a small strip on the medial aspect and extending from the epiphyseal plane to a point five centimetres (two inches) up the shaft. The cortex was destroyed around the whole periphery of the affected portion, whilst a soft tissue mass could be seen extending posteriorly into the popliteal space and to a slighter degree anteriorly, with osteogenic areas on both aspects. The appearance radiologically was that of a rapidly growing sarcoma.

A further radiogram of the chest did not disclose any pulmonary metastases, and on February 24 the left lower limb was amputated at a point as near as possible to the hip joint, short of disarticulation. Convalescence was uneventful and the girl went home, only to return on July 5 with urgent dyspnœa and obvious clinical signs of a large effusion of fluid in the left pleural cavity. She died a few hours after admission.

Dr. Webster exhibited specimens of (i) the primary growth, (ii) cartilaginous and ossified metastatic plaques in the diaphragm, and (iii) the thoracic viscera, showing extreme collapse of the left lung and pulmonary metastases. The intrapulmonary metastases were clearly demarcated from the lung tissue and could be easily separated from it. Very many of the deposits exhibited an umbilicated appearance; all were firm and elastic, and gave a distinct impression of chondrification. Innumerable metastatic deposits were present on the parietes of the left side of the chest, covering the dome of the pleura, the ribs and the diaphragm. They were of the general character he had described, and appeared to follow the course of the intercostal vessels. In every case the metastasis was firmly attached to the rib.

Dr. Webster remarked that in this patient the vexed question of the relationship of injury to malignant disease of bone was again introduced, and commented on the fact that such a highly differentiated neoplasm should have run such a rapid course. He exhibited photomicrographs which showed an advanced degree of chondrification, and drew attention to the fact that in the diaphragmatic deposits were masses of eburnated bone.

Chronic Osteomyelitis.

Dr. Webster then showed specimens from a child who had died at the age of one year and ten months after a protracted illness due to osteomyelitis. The original infection was located in the upper portion of the left femur, and was followed after some months by a cervical osteitis, which resulted in a retropharyngeal abscess. This was treated apparently successfully, but it became necessary to admit the baby to hospital a third time when he presented clinical signs of meningitis.

The brain was exhibited to show a large cerebral abscess in the right fronto-parietal region and purulent basal meningitis. At the autopsy the ear chambers were found to be scrupulously clean, and there were no cicatrized pulmonary infarcts or evidence of pericarditis. The left femur was slightly angulated, although there was no gross alteration of contour; there was no formation of involucrum and no sequestra remained. The femur was shown to demonstrate complete sequestration of the head and the greater part of the neck. A condition of fibrous ankylosis had been established, the acetabular cavity being filled with fibrous tissue, removal of which revealed no remains of articular cartilage.

Poliomyelitis.

Dr. Webster also discussed the pathology of poliomyelitis and illustrated his remarks with lantern slides. His address has already been published in the issue of September 11, 1937, at page 448, in the report of the special meeting of the Victorian Branch of the British Medical Association, held on July 29, 1937.

DR. JEAN MACNAMARA said that it was splendid to see the slides, some of which she recognized as those shown by Dr. Webster on a previous occasion. She had found the old ones of great help in the after-treatment of poliomyelitis. She had fixed in her memory particularly the photograph of one little cell surviving when two had died, and had derived considerable encouragement from this concept. She thought that the doctrine of axonal spread, which had been derived from experimental poliomyelitis, should be accepted with caution. Since Whitman's day clinicians had accepted the view that a general systemic infection occurred, and this view had always seemed to fit the picture. In the last decade more money had been available for experimentation in poliomyelitis, notably from President Roosevelt's Birthday Ball Funds. From work on monkeys, which had been done very carefully, the idea had developed that the disease spread along the axones. In some cases the virus had been used from monkey to monkey for many years, and it seemed to be possible to fix its effects by transmission. Dermatropic horse virus, after repeated inoculation into the nervous system, became neurotropic. In view of these facts it was necessary to be very guarded when one was asked to apply to the human being the proved facts derived from animal experimentation. Veterinarians could work with natural material; and yet the louping ill in Scotland, which was caused by a very neurotropic virus, was a systemic disease in the majority of sheep, but in exceptional cases, when the virus "spilt over", it was a nervous disease.

Dr. Macnamara said that one difficulty she had had in accepting the old view of the path of infection in poliomyelitis was that the virus should have been found in the cerebro-spinal fluid in the stage in which it was looked for if it was present in the cerebro-spinal fluid. She also pointed out the variations in the behaviour of the different strains of the virus. In the outbreak which occurred in Los Angeles several years previously, as in the present epidemic in Melbourne, it had been found possible to link up the cases; this was an exceedingly hard thing to do as a rule.

DR. ROBERT SOUTHBY said that the ordinary herpes virus was also capable of variation in behaviour and of assuming epidemic proportions. Dr. Duhig, of Brisbane, had noticed during a test match in that city that there was an epidemic of labial herpes amongst the adult spectators.

Dr. Webster, in reply, said that the whole question of the spread of poliomyelitis in the human body was in the melting pot. The experimental work strongly supported

the theory of axonal spread. Efforts were being made to prove that epidemic encephalitis was due to a special strain of herpes virus.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Carlton, on August 11, 1937, DR. A. P. DERHAM in the chair.

Continuous Negative Pressure Drainage of the Chest.

DR. E. R. TRETHEWIE, at the request of DR. J. R. WHITAKER, showed a child, aged three years and three months, who had developed acute pyopneumothorax during the third week of a left-sided pneumococcal pneumonia, and had been treated by continuous negative pressure drainage with cessation of drainage in twenty-one days. Manual intermittent suction, with the tube led under water, was employed for the first few days till the lung perforation had healed, and then negative pressure was increased gradually to 275 millimetres (eleven inches) of mercury. The tubing was arranged as described by Dr. J. I. Hayward (*Royal Melbourne Hospital Clinical Reports*, Volume VI, December, 1935, page 63), but pressure tubing was used. The patient's temperature fell dramatically to the normal level immediately after operation and rose only to between 37·25° C. and 37·8° C. (99° and 100° F.) during the second week. Thereafter it had remained practically normal. One month after operation the child was discharged from the ward with the wound healed and the lung fully expanded. Three months had elapsed at the time of the meeting, and the child had remained well and there had been no discharge from the wound. Dr. Trethewie demonstrated the skiagrams, in which it could be seen that the lung had been kept expanded continually until after the perforation had closed.

Dr. Trethewie discussed the evolution of continuous negative pressure drainage through the stages of open drainage (of necessity dependent drainage with thick pus) to "tube under water" drainage (feasible at an earlier stage), and to continuous negative pressure drainage in order to maintain the cavity continuously empty (valid from the time of diagnosis of an empyema). He stressed the necessity for greater suction than had been employed hitherto. This had been suggested to him originally by Dr. E. S. J. King. Four, five or six inches of mercury pressure were required, but even eleven inches, as in the patient shown, might be needed. The use of pressure tubing followed as a corollary. The method of fixing the tube into the chest, to allow of ready examination of the site of the incision without disturbance of the tube, and of the manipulation of the negative pressure, was demonstrated. (J. I. Hayward and E. R. Trethewie, *Royal Melbourne Hospital Clinical Reports*, Volume VIII, Number 1, June, 1937, page 42.)

Dr. Trethewie also showed skiagrams of a left-sided double encysted empyema in an adult patient, and of a left-sided acute pyopneumothorax following bronchopneumonia in a two-year-old child, in which could be seen the failure of closed drainage when the tube was inserted in the lower limit instead of into the centre of the cavity. In the former case central insertion as a subsequent procedure had resulted in the rapid clearance of the empyema within thirty-six hours, but in the latter case, though the chest was emptied of pus after the second operation, the child had died. At autopsy the mediastinum was found to be rigidly fixed in the right side of the chest through gross and firm adherence to the hardened left lung.

The ascent of the diaphragm, especially in closed negative pressure drainage, obliterated the lower portion of an empyema cavity, and the remainder was obliterated concentrically towards the drainage point. These facts were explained by Dr. Trethewie by means of diagrams, and he also mentioned the diminished necessity for irrigation of the cavity when drainage was adequate, and the importance of careful percussion of the chest throughout the course of the treatment, to exclude the presence of other collections, and to follow the progress of the emptying of the cavity that was being drained.

DR. J. R. WHITAKER stated that he had been gratified with the results of drainage by means of the apparatus which Dr. Trethewie had introduced into use at the Children's Hospital, and he felt sure that it was an advance on previous methods. With this in mind he had asked Dr. Trethewie to arrange the present demonstration for the information of the members of the society.

DR. W. R. FORSTER congratulated Dr. Trethewie on the admirable manner in which he had presented the subject of closed drainage by the improved method, and said that it was evident that the intelligent cooperation of the members of the nursing staff was of great importance. It appeared to him that the method could not be applied satisfactorily unless a portion of a rib was resected to provide an opening in which the tube would sit snugly.

Rheumatic Nodules.

DR. J. W. GRIEVE showed two patients with rheumatic heart disease, with the object of drawing attention to the rheumatic nodules present. One patient was a boy, aged twelve years, who had been originally admitted to hospital on April 27, 1936, with rheumatic heart disease. He was readmitted to hospital on July 6, 1937, on account of pyrexia and pains in the chest. The heart was enlarged, and a slight mitral systolic murmur was noted which was conducted to the axilla. Skin nodules were noticed, first on the volar surface of each wrist; these nodules had increased in size, and many large nodules had become palpable over the occipital region, and some were found on the feet. The heart affection had progressed, and evidence was obtainable of mitral and aortic valvular lesions.

The other patient shown by Dr. Grieve was a girl, aged nine years, who had been admitted to the hospital on December 2, 1936, with rheumatic fever. Periarticular lesions predominated at first, but she was dyspnœic and contracted pericarditis while in hospital. On December 20, 1936, she was transferred to the after-care home, and had made slow progress there until, on becoming feverish again, she was returned to the hospital at the commencement of the month of August, 1937. When she was examined soon after the original admission to hospital, the heart was found to be enlarged. The apex beat was located in the sixth left intercostal space, 9·37 centimetres (three and three-quarter inches) from the mid-line of the sternum. It was estimated that there was one and a half fingers' breadth of cardiac dulness to the right of the sternum. A systolic murmur was heard readily over the mitral area. There was some evidence of cardiac failure; the liver was enlarged downwards; there was slight dulness at the base of the right lung and a little ascites was present. The sedimentation rate at that stage showed a fall of twelve millimetres in one hour. It was realized that the fall would have been greater in the absence of heart failure. Skin nodules were present on the hands, elbows and knees. A short diastolic bruit had become audible recently.

Dr. Grieve stated that rheumatic nodules were found not infrequently and a search should always be made for them. There had been an unusual number of patients in the hospital that year with rheumatic affections, and more examples than usual of rheumatic nodules had been seen. He was inclined to correlate the rise in the incidence and the economic depression through which the community had just passed. Dr. Grieve considered that the finding of nodules was of importance, because it almost invariably indicated active involvement of the heart by the rheumatic infection. The common sites of the nodules were over the bony prominences and the tendons. The common sites were the olecranon, the knuckles, the patella, the malleoli, the vertebral spine, the scapulæ and the occiput. Sometimes only one nodule was found, but often twelve or more could be seen. They usually came in crops, and might appear in the course of a few days. They were painless, and the size varied from that of a pin's head to that of a pea; they were apt to be largest over the occiput. The duration of the nodule was two or three weeks as a rule, but they might last for months and become fibrous. Dr. Grieve commented on the prognostic value of rheumatic nodules. He said that they were

always indicative of activity of the infection. If they occurred at the onset the prognosis was very grave; the children often died within a few years. If they occurred during the course of the disease, this fact rendered the prognosis graver. In the series of sixteen patients exhibiting nodules reported by Carey Coombs, ten had died at an average time of five and a half years after the appearance of the nodules, and the remainder were seriously crippled at the end of fifteen years. Dr. Grieve classified the gravity of rheumatic affections according to the type of onset. The prognosis was worse if the onset was associated with nodules, not so serious with carditis; with polyarthritis it was less serious, and it was best of all with chorea.

Tuberculous Bronchopneumonia with Cavitation.

DR. V. L. COLLINS, on behalf of DR. E. M. TYMMS, showed a girl, aged twelve years, who had been admitted to hospital on June 8, 1937, from an institution in which she had lived for about six years. Nothing was known of the details of her health before she entered the institution, but it was stated that she had not had any illness since until she contracted a severe cold one month before admission to hospital. She had remained in bed for a week and later had returned to school; but four days before her admission to hospital, on account of pyrexia in the latter part of the day and persistence of the cough, together with night sweats, poor appetite and loss of weight, she consulted the doctor again. When she was examined in hospital, the temperature was slightly raised and the percussion note was impaired at the left apex; the breath sounds were vesicular at the base; there was diminution of the vesicular murmurs anteriorly towards the left apex; and rhonchi were audible posteriorly on each side. Infiltration involving the upper section of the left side of the chest was reported by the radiologist, and after a lateral skiagram had been prepared it was added that the appearances were those of a possible lung abscess involving the left upper lobe. The illness followed a pyrexial course and the patient was frequently troubled with cough, but she did not produce much sputum. The general condition remained fairly good and the appetite was satisfactory; but on July 20 it was noted that distant tubular breathing and relative dulness to percussion had been found at the right apex and high in the axilla. A radiographic examination after instillation of lipiodol was carried out on August 5, but, though some lipiodol reached the upper lobe, there was no definite visualization of the filling of the cavity. There was a positive response to the von Pirquet test and a weak positive response to the Mantoux skin test was obtained on two occasions. There was no reaction to the Casoni skin test, and no tubercle bacilli had been found on repeated searching of specimens of the sputum. The appearance of the vocal cords was normal. In spite of postural treatment the child had produced only a few drachms of sputum daily.

DR. E. M. TYMMS said that his first impression was that the girl was tuberculous, but, although she was troubled much by coughing, there had never been any expectoration, and this feature was rather difficult to reconcile with a diagnosis of pulmonary tuberculosis. The radiograms had been closely studied, and it was assumed that, following bronchopneumonia or possibly the inhalation of a foreign body, cavitation had developed but had remained closed. The girl had never had much fever and did not seem to be very ill. The cutaneous tests for tuberculosis had resulted in a definite positive finding to the von Pirquet test and a weakly positive reaction to the Mantoux test. One week prior to the meeting signs of bronchitis developed in the other side of the chest, but the girl's general condition seemed no worse. A radiological examination after the introduction of lipiodol under local anæsthesia by Dr. Collins showed that none of the lipiodol reached the cavity, confirming the opinion that it was a closed cavity. The question of endoscopy had been considered, but as yet no action had been taken in this direction. Undoubtedly many non-opaque foreign bodies could cause a pulmonary abscess, and the diagnosis resolved itself into a consideration of what was the most probable ætiology of a localized pulmonary abscess, other than tuberculosis.

DR. KEITH HALLAM discussed the several types of lung abscess and their radiological differentiation. Such an abscess might be a sequela of a condition such as pneumonia, tuberculosis or cancer. Or again, it might arise by extension from a neighbouring infective process, such as a subphrenic abscess. A third type was the aspiration abscess, and a fourth type the metastatic or embolic abscess. There were also to be considered hydatid cysts and solitary congenital cysts of the lung. On radiological grounds he was inclined to eliminate the first two types. Aspiration abscesses were usually in one of the smaller bronchi, but the possibility of a metastatic abscess had to be admitted, and a solitary cyst of the lung could not be excluded. On radiographic grounds he favoured infection in a congenital solitary cyst of the lung as the diagnosis.

DR. A. P. DERHAM pointed out that the child had been for five years in an institution and no family history was obtainable. In the same institution a child had been considered to be suffering from pulmonary tuberculosis. Tuberculosis as the diagnosis in Dr. Tymms's patient was therefore not to be discarded too readily.

Dr. Collins, in reply, said that failing tuberculosis he had been obliged to postulate some curious cyst which demanded investigation and possibly endoscopy. There were now definite signs of bronchitis and alveolitis in the opposite side of the chest, and a radiogram taken the day preceding the meeting showed a mottling in the upper lobe of the right lung which strongly suggested tuberculosis. It now appeared that the closed cavity in the upper lobe of the left lung was of tuberculous origin, that it had been activated by the injection of lipiodol and occasioned what he presumed to be a tuberculous bronchopneumonia. He had withheld the last radiogram, as he was desirous of securing discussion on the condition as he had seen it during the previous week.

Giant Diverticulum of the Bowel.

DR. REGINALD WEBSTER showed a specimen of a giant diverticulum of the bowel in a baby. A report of this case is to be published in a later issue.

Correspondence.

TUBERCULOSIS.

SIR: My name has recently appeared in the letters to the journal concerning the use of tuberculin and referring to some remarks made by me at the Adelaide congress, which have been obviously misunderstood. I did not discuss the present-day therapeutic use of tuberculin, of which I have had very little experience. I only spoke to make two suggestions: Firstly, that a diagnostic injection of tuberculin should never be given without a previous X ray examination of the lungs, and I mentioned a case where catastrophe followed such omission. Secondly, I made the suggestion that doctors should report disasters. Although the case mentioned was used as an illustration, I was referring to medical and surgical practice in general, and in using the word disaster I did not mean only deaths. I have made this latter suggestion previously, but on each occasion it appeared to cause amusement. I do not know why it should. There would be no need for the medical man's name to appear, nor any reference to the identity of the patient or any institution.

Some of these happenings come before coroners, some before medical defence bodies; it is only reasonable to suspect that there are many others which do not come before either, and even those which do may not reach our medical journals.

The younger generation should be given the opportunity of learning from the mistakes of their elders, otherwise those mistakes will continue to be repeated, as one in a long medical life has so often seen.

Yours, etc.,

ARTHUR PALMER.

50, Prince Albert Street,
Mosman,
New South Wales.
December 7, 1937.

Books Received.

APPLIED PHARMACOLOGY, by A. J. Clark, M.C., M.D., F.R.C.P., F.R.S.; Sixth Edition; 1937. London: J. and A. Churchill Limited. Demy 8vo, pp. 688, with 83 illustrations. Price: 18s. net.

DISEASES OF THE SKIN: A MANUAL FOR STUDENTS AND PRACTITIONERS, by the late R. W. MacKenna, M.A., M.D., Ch.B.; Fourth Edition, revised and enlarged by R. M. B. MacKenna, M.A., M.D., M.R.C.P.; 1937. London: Baillière, Tindall and Cox. Royal 8vo, pp. 572, with 168 illustrations and 46 coloured plates. Price: 20s. net.

THE EDUCATION OF THE EMOTIONS THROUGH SENTIMENT DEVELOPMENT, by M. Phillips, M.A.; 1937. London: George Allen and Unwin Limited. Large crown 8vo, pp. 318. Price: 8s. 6d. net.

MOTHERCRAFT, ANTENATAL AND POSTNATAL, by R. C. Jewesbury, M.A., D.M., F.R.C.P.; Second Edition; 1937. London: J. and A. Churchill Limited. Demy 6mo, pp. 197, with 21 illustrations, of which 13 are in colour. Price: 10s. 6d. net.

COLLECTED PAPERS OF THE SCHOOL OF PUBLIC HEALTH AND TROPICAL MEDICINE, THE UNIVERSITY OF SYDNEY; Volume I; 1937. Australia: The Commonwealth Department of Health and the University of Sydney. Demy 4to, with illustrations.

THORACIC SURGERY, A REVISED AND ABRIDGED EDITION OF SAUERBRUCH'S DIE CHIRURGIE DER BRUSTORGANE, by F. Sauerbruch and L. O'Shaughnessy, F.R.C.S.; 1937. London: Edward Arnold and Company. Double demy 9mo, pp. 402, with illustrations. Price: 50s. net.

DRUG ATLAS FOR STUDENTS OF PHARMACY AND MEDICINE, compiled by W. S. Lean, B.Pharm., Ph.C.; 1937. London: Longmans, Green and Company Limited. Demy 4to, pp. 16. Price: 2s. 6d. net.

PRIMITIVE INTELLIGENCE AND ENVIRONMENT, by S. D. Porteus, D.Sc.; 1937. New York: The Macmillan Company. Demy 8vo, pp. 334. Price: 15s. net.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY, by H. Bailey, F.R.C.S.; Sixth Edition, revised; 1937. Bristol: John Wright and Sons Limited. Medium 8vo, pp. 296, with 358 illustrations, some of which are in colour. Price: 21s. net.

CHEMICAL METHODS IN CLINICAL MEDICINE: THEIR APPLICATION AND INTERPRETATION, WITH THE TECHNIQUE OF THE SIMPLE TESTS, by G. A. Harrison, B.A., M.D., B.Ch., M.R.C.S., L.R.C.P.; Second Edition; 1937. London: J. and A. Churchill Limited. Medium 8vo, pp. 596, with 3 colour plates and 86 illustrations. Price: 21s. net.

Diary for the Month.

DEC. 21.—Tasmanian Branch, B.M.A.: Council.
DEC. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
DEC. 30.—South Australian Branch, B.M.A.: Branch.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum *tenentes* sought, etc., see "Advertiser," pages xviii to xxi.

METROPOLITAN INFECTIOUS DISEASES HOSPITAL BOARD, ADELAIDE, SOUTH AUSTRALIA: Resident Medical Officer.
THE QUEEN'S (MATERNITY) HOME INCORPORATED, ROSE PARK, SOUTH AUSTRALIA: Resident House Surgeon.
THE UNIVERSITY OF MELBOURNE, VICTORIA: Staff Vacancies.
WYALCATCHEM ROAD BOARD, WYALCATCHEM, WESTERN AUSTRALIA: Medical Officer.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135 Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178 North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

Editorial Notices.

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